BRIEF COMMUNICATION

Octreotide for enterocutaneous fistulas of Crohn’s disease

A Lavy MD1, K Yasin MD2

Crohn’s disease is a chronic, life-long disease and has many troublesome complications. Fistulas are a part of Crohn’s disease, and although there are many therapeutic modalities used in treating these fistulas they are only partially successful. As we are still very far from being able to cure it, the aim is to improve the patients’ quality of life and to reduce the iatrogenic harm that may be caused by various treatment modalities. Somatostatin is an inhibitor of intestinal secretion and has been used to treat pancreatic and surgical fistulas. Therefore, we decided to treat enterocutaneous fistulas using somatostatin.

METHODS: Five patients with Crohn’s disease were treated with four daily injections of 300 µg octreotide. The total period of treatment was eight weeks.

RESULTS: Closure of fistulas was achieved in four of the five patients.

CONCLUSION: Somatostatin may have a role in treating Crohn’s disease enterocutaneous fistulas and may prevent surgery or prolonged immunosuppressive therapy.

Key Words: Crohn’s disease; Enterocutaneous fistulas; Octreotide

Fistulas are a part of Crohn’s disease presentation. They are considered in three categories (1-7):
1. Benign or innocent;
2. Mild or “nuisance”; and
3. Complicated, associated with an abscess or intractable bowel disease.

Fistulas of the first category usually do not require treatment. Fistulas of the third category are mostly treated surgically (8). As for the second category, there are many therapeutic modalities with only partial success. Included in this category are enterovesicular, enterocutaneous and enterocolic fistulas. Most are treated with antibiotics and immunosuppressive drugs (9-13) for many months to achieve any result. For most of modalities the response rate is up to 60%, but relapse is common (14). Infliximab was shown to be effective in 67% of cases (15) but again, relapse rate is high because many patients develop tolerance or side effects. Results are somewhat better (14) but again, relapse rate is high because many patient

Because somatostatin is an inhibitor of intestinal secretion (21-23) and has been tried in a wide variety of medical conditions (24-29) including pancreatic and surgical fistulas (30-33), we decided to use a relatively high dose to treat Crohn’s disease enterocutaneous fistulas.

PATIENTS AND METHODS

Five patients with Crohn’s disease and enterocutaneous fistulas were treated with octreotide. Each patient served as his own control, having each been treated with mesalazine and metronidazole

©2003 Pulsus Group Inc. All rights reserved
before. The patients were taught to subcutaneously inject 300 µg of octreotide four times daily. The dose was chosen according to previous partially successful reports for surgical fistulas (27-29). To demonstrate effect, we decided to give a relatively high dose in this pilot study. The patients were seen every week by the same physician and fistula was assessed according to pads used by the patient.

Other medications, including antibiotics, were not allowed. The total period of treatment was eight weeks. Results are shown in Table 1 and case reports are described below.

### CASE PRESENTATIONS

**Case one**
A 17-year-old girl developed Crohn's disease of the terminal ileum at the age of 15. She was well on mesalazine for two years and then developed fever and a red tender spot in the right groin. Computerized tomography revealed inflamed small bowel loops with an abscess formation. This was punctured for drainage and later an enterocutaneous fistula developed. The patient was treated for three months with corticosteroids, ciprofloxacin, metronidazole and mesalazine, without response. She was then put on total parenteral nutrition for bowel rest, and after an additional two weeks, injections of somatostatin were added. Four weeks of treatment closed the fistula. Two weeks later an upper gastrointestinal series was done, following which the fistula reopened. She was sent for surgery and had terminal ileectomy. Since then, she has been doing well solely on mesalazine.

**Case two**
A 50-year-old man had Crohn's disease for 30 years. Five years after diagnosis, he had a terminal ileectomy and a right hemicolectomy due to obstructive disease. Twelve years later he had another resection of the preanastomotic intestine for the same reason, following which an enterocutaneous fistula developed. He was treated with mesalazine, metronidazole, corticosteroids and 6-mercaptopurine for six months without improvement. Somatostatin was then added. The fistula closed after five weeks and has remained closed for 24 months. The patient is currently taking mesalazine and 6-mercaptopurine.

**Case three**
A 40-year-old man was suffering from diffuse Crohn's disease for 26 years. At the age of 14 years he had a subtotal colectomy, followed by a short remission.

A year later he was sick again, necessitating prolonged periods of corticosteroids and mesalazine. An attempt to give him 6-mercaptopurine led to severe neutropenia. There was no response to methotrexate. At 21 years of age he underwent his second surgery, a gastrojejunostomy, because of obstruction due to Crohn's duodenal involvement.

Two years later he developed severe perianal disease and twice had perianal abscess drainage. At that time, he already had an anastomotic stricture, which was dilated at colonoscopy using through-the-scope balloon dilators. He developed an enterocutaneous fistula, originating in the preanastomotic ileum. He did not respond to three months of treatment with metronidazole and corticosteroids and was therefore started on somatostatin injections. After three weeks, the fistula closed. He completed eight weeks of treatment. The fistula has remained closed for 19 months, and the patient is currently taking mesalazine and intermittent corticosteroids.

**Case four**
A 37-year-old man was diagnosed as suffering from Crohn's disease involving most of the ileum. He was treated with mesalazine, but a year later he was hospitalized with fever and pain. Computerized tomography revealed abscess formation above the bladder. This was drained and he received antibiotics, corticosteroids and mesalazine. Removal of the drain resulted in ileocutaneous fistula formation. After two months of metronidazole, somatostatin injections were added and the fistula closed within two weeks. The patient completed eight weeks of treatment. He was maintained on mesalazine, but a year later his disease worsened and the fistula reopened. At
that time he was referred for surgery and had a resection of the cecum and a segment of distal ileum. He recovered uneventfully.

Case five
A 45-year-old man was suffering from Crohn’s disease for six years. He had involvement of the terminal ileum and rectum together with an active perianal disease. He was treated with mesalazine, metronidazole and 6-mercaptopurine for six months, but developed a cologluteal fistula.

He was started on somatostatin injections and his gluteal fistula closed after six weeks. The patient complained of worsening diarrhea, but was able to complete eight weeks of treatment. The fistula has remained closed for twelve months, and the patient is currently taking mesalazine and 6-mercaptopurine.

Patient compliance and side effects
The patients were taught to inject themselves with somatostatin four times daily, and complied very well. Most of them tolerated the treatment well. Patient five complained of increased stool frequencies during treatment but he still completed eight weeks of therapy.

Acknowledging the reported complication of gallstones in patients receiving somatostatin (27-28), all patients were followed by an ultrasonographic examination. None developed gallstones. However, because of this feared complication, we chose not to prolong treatment beyond eight weeks.

DISCUSSION
Somatostatin is a cyclic peptide, consisting of 14 amino acids (31) with a variety of physiological activities. It is a neurotransmitter in the central nervous system and regulates growth hormone and thyrotropin release.

In the gastrointestinal tract, somatostatin has a mainly inhibitory action on glandular secretion, smooth muscle contractility, absorption of nutrients and activation of immune cells, as well as pancreatic secretion (34-35). It has been clearly shown to be present in inflammatory tissues.

Because of these qualities, somatostatin may be suitable for treating high to moderate output fistulas, which are troublesome to the patient. Several studies reported favourable results for both small bowel and pancreatic postoperative fistulas (36-38). In 1993, Torres et al (39) reported a double-blind study with 40 patients which found no significant difference in the percentage of fistula closures, following somatostatin treatment.

REFERENCES

Octreotide for enterocutaneous fistulas of Crohn’s disease
Fistulas are common and occur in up to 35% of patients with Crohn’s disease. They are very troublesome to the patient and markedly reduce quality of life; therefore, there should be a place for less toxic therapy such as somatostatin, whether as a single symptom. In a pilot study, we treated five Crohn’s disease patients with enterocutaneous fistulas, giving relatively high doses of octreotide, the potent analogue of somatostatin (45), and four of them responded.

We suggest that somatostatin may have a role in treating Crohn’s disease enterocutaneous fistulas and may prevent surgery or prolonged immunosuppressive therapy. Longer treatment should be considered as well as long-acting somatostatin analogues in an aim to achieve better results.
Lavy and Yasin
