CASE REPORT

Octreotide Acetate To Treat Pancreatic Fistula

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CASE

A 58-year old woman was transferred to our facility after sustaining multiple injuries in a motor vehicle accident. At the time of the accident, the patient was wearing a lap belt and sustained major blunt abdominal and chest trauma.

On physical examination the patient was noted to have facial abrasions, bruising of the left chest wall, abdominal bruising, tenderness below the umbilicus and neck pain in the region of C5 - C6. Vital signs were, blood pressure 92/60 mmHg, pulse 70, respirations 16 breaths/minute and temperature 37°C. The patient's CBC, serum electrolytes, PT and PTT were normal. Lactate dehydrogenase was 286 u/L, aspartate transaminase 147 u/L, creatine kinase 177 u/L and amylase greater than 200 u/L. Chest X-rays demonstrated a fracture of ribs #9, 10, 11 and spine X-rays suggested a teardrop fracture of C5 with increased pre-cervical swelling, later demonstrated to be negative by CT scan. Diagnostic peritoneal lavage was attempted but was unsuccessful due to a huge hematoma cavity between the abdominal fascia and subcutaneous tissue. Emergency laparotomy was performed and revealed a massively contused head of the pancreas, small bowel and large bowel. The central retroperitoneal hematoma was explored and drained, the peritoneum lavaged and suction drains were placed posteriorly and anteriorly to the pancreas.

Post-operatively the patient did extremely well and within one week the drains had been removed. The patient was comfortable and diet as tolerated was started. However, on the seventh post-operative day, one of the drain sites began to drain substantial volumes of serous fluid which was determined to contain almost exclusively amylase. An endoscopic retrograde cholangiopancreatogram was performed and identified an incomplete disruption in the pancreatic duct five centimeters distal to the ampulla of Vater. A colostomy appliance was placed over the fistula site and drainage steadily increased over the next three days, at which time greater than 700mL of amylase rich fluid was removed for each 24 hour period. Oral intake was discontinued, central TPN initiated and octreotide acetate 100 mcg SC TID was prescribed. Within 24 hours fistula output had drecreased to 235 mL/day. The patient was maintained on octreotide over the next 15 days until the time of discharge. During this time, fistula output continued to decline (Table I), oral intake was resumed and the patient was discharged with no demonstrable complications.

Table I: Octreotide's effect on fistula output

Post-Op Day		Output (mL/24h) from drain site
1		75
5		0
11	*octreotide started*	>700
12		235†
26		drops

† 66% decrease in fistula output within 24 hours.

DISCUSSION

The term 'fistula' simply refers to an abnormal passage or tract leading from one hollow organ to either another hollow organ or the exterior. In the GI tract, fistulae often result from surgery, accidental trauma, malignancies, Crohn's disease, radiation therapy or infection. This case demonstrates a classic example of pancreatic fistula formation following blunt traumatic injury to the pancreas. The development of a pancreatic or small bowel fistula (Figure 1) is almost always associated with trauma to the pancreas or small bowel, often as a result of surgery. Subsequent to fistula formation, the continuous flow of pancreatic digestive polypeptides and in the case of small bowel fistula, also gastric acid, function to inhibit and delay closure of the fistula. As a result, the fistula may remain patent for months. During this time, serious complications

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The authors would like to acknowledge: C.D. Bayliff, Pharm.D. for his review of the manuscript and Mrs. Jan Butler for her secretarial assistance.

such as infection, hemorrhage, erosion to adjacent viscera, fluid and electrolyte imbalance and malnutrition[1] can develop. Standard therapy for managing both pancreatic and small bowel fistulas includes withholding oral intake, fluid replacement, correcting electrolyte disturbances and providing adequate nutrition via parenteral alimentation or tube feedings.[2]

Any pharmaceutical agent which is capable of facilitating fistula closure, thereby reducing the potential for complications, reducing hospital stay and possibly avoiding surgical intervention, would be a welcome addition to medical management of this condition. Both somatostatin (a naturally occurring polypeptide found in a number of areas in the body, most notably the pancreas and hypothalamus) and octreotide acetate (a longer acting synthetic analogue of somatostatin marketed under the trade name, *Sandostatin®*) are potent inhibitors of gastric and pancreatic secretions.[3,4] The effects of octreotide acetate on fistula output in this case support the findings of other studies using either somatostatin[5,6] or octreotide[7,8] and would suggest that these agents, in addition to standard accepted methods, do in fact facilitate fistula closure. A single, randomized, double blind, cross-over study[9] demonstrated the effectiveness of octreotide (225 - 300 mcg/day) in significantly reducing output from small bowel fistula in 14 of 14 patients (from a mean of 828 to 247 mL/day after one day of therapy) compared with placebo. In addition, 11 of the 14 fistulas had spontaneously closed following two to ten days of octreotide therapy.

Without somatastatin or octreotide therapy, many pancreatic and small bowel fistula will eventually close spontaneously, however, this often takes weeks to months.[8,9,10] While prospective controlled trials investigating the usefulness of octreotide in facilitating pancreatic fistula closure have not been conducted, growing experience gained from isolated case reports and retrospective reviews strongly support the benefits this agent can offer in this particular setting. As a result of octreotide's widespread gastrointestinal actions, pharmacists should be aware of its

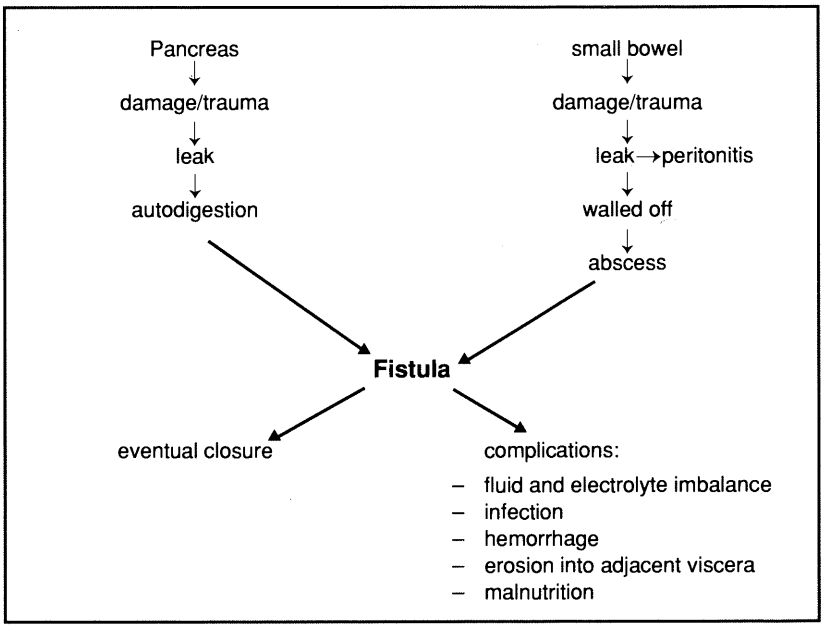

Figure 1: Fistula Formation

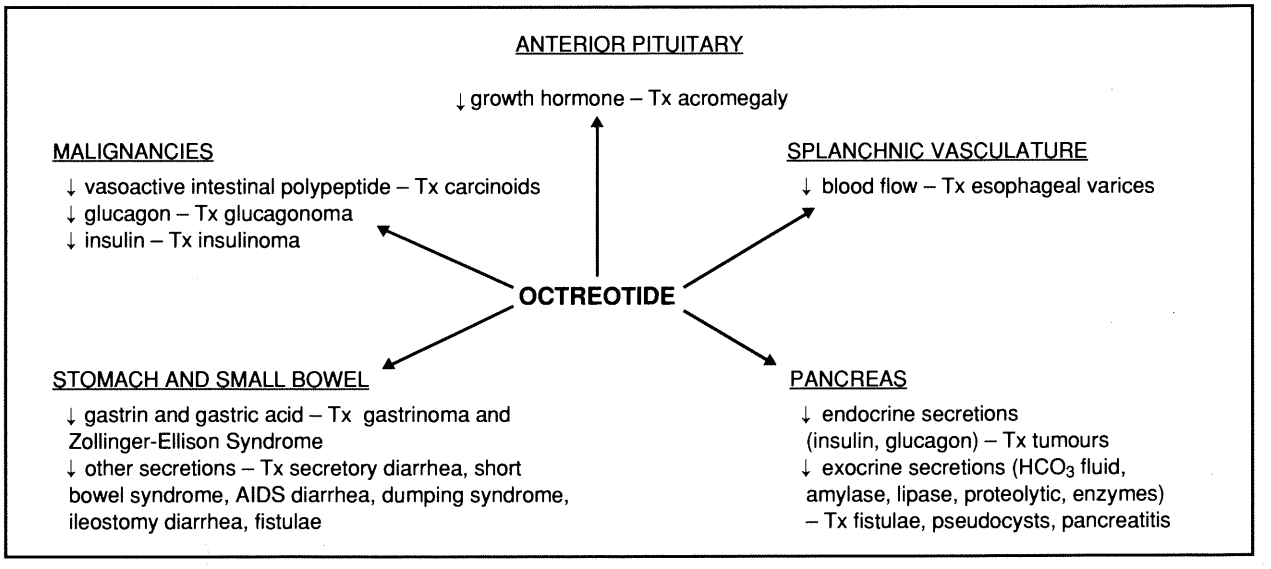

Figure 2: Actions and Potential Indications

potential use in the medical management of a number of gastrointestinal conditions, some of which would otherwise necessitate surgical intervention (Figure 2). The exact role octreotide will play in the pharmacotherapy of these conditions requires further study.

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