Dramatic Effect of a Somatostatin Analogue in Decreasing Mucus Production by the Intestinal Segment After Enterocystoplasty

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Purpose: Catheter obstruction from mucus plugging and urinary leakage are common problems after enterocystoplasty. A large suprapubic catheter and frequent bladder irrigation with normal saline are routinely used in the postoperative period to decrease catheter plugging. In this study we evaluated the use of a somatostatin analogue (Sandostatin®) to decrease mucus production by the intestinal segment after enterocystoplasty.

Materials and Methods: We performed enterocystoplasty using ileal segments (20 to 30 cm) in 40 patients. In 20 patients Sandostatin (0.05 mg subcutaneously) was started 1 hour before the procedure and was then administered every 8 hours for 15 days. Bladder irrigation was performed whenever drainage from the suprapubic catheter caused blockage. The drain was removed 24 to 48 hours after the resumption of oral feeding if urine leakage was insignificant. We then compared the number of bladder irrigations required, mucus volume, time to remove the drain and hospital stay between the groups.

Results: Only 5 patients in the treatment group required bladder irrigation. The mean number of bladder irrigations for each patient was 0.35 ± 0.67 in the group receiving Sandostatin and 10.35 ± 2.13 for the control group ($p < 0.001$). Mean mucus volumes on postoperative day 3 were 4.42 ± 1.95 and 42.5 ± 5.14 ml in the treatment and control groups, respectively ($p < 0.001$). Mean time to remove the drain was 6.35 days for the Sandostatin group and 6.8 days for the control group. Mean hospital stay was 7.4 and 7.9 days for the treatment and control groups, respectively ($p < 0.05$).

Conclusions: Sandostatin caused a marked decrease in mucus production by the intestinal segment with patients receiving Sandostatin no longer requiring routine postoperative bladder irrigation and having a shorter hospital stay.

Key Words: mucus, catheterization, urinary bladder, intestinal secretions, octreotide

Enterocystoplasty is the standard treatment for patients with decreased bladder compliance or functional capacity due to neurogenic bladder who do not respond to nonsurgical treatments (such as anticholinergic drugs and CIC). The objective is to reach a bladder with acceptable volume and compliance without increasing intravesical pressure.[1–4] Various segments of the gastrointestinal tract such as ileum, colon and stomach have been used for enterocystoplasty. One of the bothersome problems after this operation is mucus production,[2,5] which can result in obstruction of the suprapubic catheter with ensuing urine leakage from suture lines, infection, fistula, suture dehiscence and other postoperative complications.[1–4] Therefore, the bladder is drained with a large bore suprapubic catheter postoperatively which must be irrigated at least 3 times daily and whenever drainage decreases.[6] Catheter occlusion and repeated bladder irrigation increase the risk of infection and urinary leakage. In addition bladder irrigation should be performed by an experienced nurse or resident. Somatostatin, a peptide hormone with 14 amino acid residues, strongly inhibits intestinal secretions.[7–10] Considering this potentially beneficial effect in the setting of enterocystoplasty we studied the efficacy of Sandostatin (octreotide acetate, a somatostatin analogue) in decreasing intestinal segment mucus production after enterocystoplasty.

METHODS

From September 2005 through February 2008, 40 enterocystoplasty candidates were assigned by balanced randomization to control or treatment groups. The patients with odd numbers were included in the treatment group and those with even numbers in the control group. This process went on for 40 samples and informed consent was also obtained. Surgery was conducted to preserve the upper urinary tract and to prevent progressive damage. In 2 patients surgery also was conducted to retain continence.

In both groups a 20 to 30 cm segment from the ileum at least 15 cm from the ileocecal valve was used. It was reconfigured to cup patch or U shape, and then the bladder was bivalved and anastomosis was performed with absorbable sutures. A 24Fr suprapubic catheter was brought out through native bladder. Patients in the control group received wide spectrum antibiotics while those in the treatment group received Sandostatin as well, which was administered subcutaneously as 0.05 mg every 8 hours with the first dose given 1 hour before the procedure. Sandostatin was continued for 15 days after the operation. If a patient was discharged home earlier than 15 days treatment was continued at home with a lower dose (0.05 mg every 12

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hours). A nasogastric tube was inserted only if abdominal distention did not resolve after medical treatment. An attending physician or a senior urology resident examined the patients 4 times daily during the hospital stay. The bladder was irrigated with normal saline only if urine drainage from the suprapubic catheter was blocked. Urine and irrigation fluid were collected for 24 hours on postoperative day 3 and the volume of mucus sediment in the collection container was measured. Oral feeding was resumed from postoperative day 5 if bowel sounds were present. The drain was removed 24 to 48 hours after oral feeding if urine leakage was minimal. Patients were instructed to perform bladder irrigation as necessary at home and were discharged from the hospital when they were able to tolerate oral feeding. The suprapubic catheter was removed on postoperative day 20 and the patients began intermittent catheterization. Duration of hospital stay, frequency of catheter obstruction requiring irrigation while hospitalized, time to drain removal and postoperative complications such as fever, urinary fistula and abdominal distention requiring nasogastric tube drainage were recorded and compared between the 2 groups. Finally the t test was used to analyze the data with $p < 0.05$ considered statistically significant.

RESULTS

All 40 patients were adult men undergoing enterocystoplasty for spastic neurogenic bladder after spinal cord injury. Mean patient age in the control and treatment groups was 38.5 and 41 years, respectively. In the control group mean length of the ileal segment was 36.25 ± 3.27 cm vs 25.35 ± 2.81 cm in the treatment group ($p = 0.357$). Average mucus volumes on postoperative day 3 in the control and treatment groups were 42.15 ± 5.14 ml and 4.42 ± 1.95 ml, respectively ($p < 0.001$). During hospitalization the mean number of required irrigations for each patient was 10.35 ± 2.13 and 0.35 ± 0.67 in the control and treatment groups, respectively ($p < 0.001$). The average time to remove the drain in the control and treatment groups was 6.8 ± 0.89 and 6.35 ± 0.58 days, respectively ($p = 0.069$). Average hospital stay in the control and the treatment groups was 7.9 ± 0.85 and 7.4 ± 0.68 days, respectively ($p = 0.048$). Return of bowel sounds in the control and treatment groups took 4.6 ± 0.6 and 4.2 ± 0.7 days, respectively. In the control group 9 patients required nasogastric drainage postoperatively vs none in the treatment group. Sandostatin was tolerated well in all 20 patients, and fortunately there were no observed and significant complications in the patients.

DISCUSSION

Mucus production occurs commonly after enterocystoplasty and can give rise to early or late complications. Early in the postoperative period mucus production by the intestinal segment leads to catheter obstruction, urine leakage and an increased risk of infection.[1,3,4] In the long term it can lead to an increased risk of urinary infection, stone formation and difficulty performing CIC.[3,4,11] There is a considerable variation in the amount of mucus produced by cystoplasty and averages 37 gm daily.[12] Attempts have been made in animal studies to eliminate mucus production by removing the intestinal mucosal layer and using the seromuscular layer of an intestinal segment,[13–15] which has also been reported in humans.[16] A bladder acellular matrix graft has also been used in animal models.[17,18] There are also reports on the use of medications such as N-acetylcysteine and urea to dissolve the mucus and, thus, decrease long-term complications in patients who perform CIC.[19] However, removing intestinal segment mucosa (demucusolization) and using acellular grafts are not standard or common practice for enterocystoplasty, and the only well established way to prevent mucus plugs in the early postoperative period is repeated irrigation of the bladder with normal saline through a large bore suprapubic catheter, which can increase the risk of infection.[3,6] In one study a Jackson-Pratt drain was used for bladder drainage to prevent catheter obstruction with mucus. However, the bladder was still irrigated twice daily.[1]

Somatostatin is a peptide with 14 amino acid residues which strongly inhibits intestinal secretions.[7] It has been used to decrease intestinal secretions with no considerable adverse effects in many gasterointestinal diseases such as intestinal fistulas.[8] We used Sandostatin (a somatostatin analogue) in the postoperative period. Sandostatin exerts pharmacological actions similar to the natural hormone somatostatin. It is an even more potent inhibitor of growth hormone, glucagon and insulin than somatostatin. Like somatostatin it also suppresses the luteinizing hormone response to gonadotropin-releasing hormone, decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin and pancreatic polypeptide.

By virtue of these pharmacological actions Sandostatin has been used to treat the symptoms associated with metastatic carcinoid tumors (flushing and diarrhea) and vasoactive intestinal peptide secreting adenomas (watery diarrhea). Sandostatin substantially reduces growth hormone and/or insulin-like growth factor-1(somatomedin C) levels in patients with acromegaly.

In an elderly population dose adjustments may be necessary due to a significant increase in the half-life (46%) and a significant decrease in the clearance (26%) of the drug. In patients with severe renal failure requiring dialysis clearance was reduced to approximately half that found in normal subjects (from approximately 10 to 4.5 l per hour). The effect of hepatic diseases on the disposition of octreotide is unknown.

Sensitivity to this drug or any of its components is the contraindication. There may be a transient local reaction at the site of injection of octreotide. Systemic side effects are mainly gastrointestinal, and may include anorexia, nausea, vomiting, diarrhea and steatorrhoea, abdominal discomfort and flatulence. Administration between meals or at bedtime may reduce these gastrointestinal effects.[20,21]

We observed a remarkable decrease in mucus secretion from the intestinal segment compared to the control group. In our study average mucus volumes in the control and treatment groups were 42.15 and 4.42 ml on postoperative day 3, respectively ($p < 0.001$). The treatment group required an average of 0.35 bladder irrigations per patient while the control group required 10.35 irrigations per patient during hospitalization ($p < 0.001$). Of the 20 patients who received this medication 15 did not need any irrigation at all. Irrigation was performed just once in 3 patients and only twice in 2 patients during hospitalization. As bladder irrigation was performed only for mucus plugging, it is evident that Sandostatin caused a significant decrease in mu-

cus secretion from the intestinal segment, reducing the need for routine frequent bladder irrigation in the early postoperative period.

Finally, hospital stay for patients in the treatment group was significantly less than that of the control group (7.4 ± 0.68 vs 7.9 ± 0.85 days, $p < 0.05$). No patient in the treatment group required a nasogastric tube postoperatively whereas 9 patients in the control group needed a nasogastric tube for abdominal distention. In the group on somatostatin not needing a nasogastric tube is a clinical finding possibly due to a decrease in bowel secretion. However, this issue is controversial and more studies should be conducted. We found no statistically significant difference in time to return of bowel sounds and tolerance of oral feeding between the 2 groups.

CONCLUSIONS

Sandostatin seems to decrease mucus secretion tremendously from intestinal segments in enterocystoplasty and, thus, reduces the need for postoperative bladder irrigation, may help decrease urine leakage and decreases hospital stay. In addition, patients who receive Sandostatin do not require nasogastric drainage in the early postoperative period. These effects translate into simpler patient care after a major urological procedure. Long-term complications of mucus production such as stone formation, urinary tract infection and poor drainage on CIC may also decrease in frequency and severity. Sandostatin may also prove useful in the postoperative care of patients with an orthotopic neobladder after radical cystoprostatectomy. The long-term indications of this medication have not yet been investigated. The research group has decided to plan an investigation on the long-term effects of somatostatin analogues on these patients.

Abbreviations and Acronyms

CIC = clean intermittent catheterization

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