

OCTREOTIDE IN THE MANAGEMENT OF ENTEROCUTANEOUS FISTULAE

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Efficacy of Octreotide (Somatostatin) in the conservative management of postoperative Enterocutaneous fistula was studied in seven patients with age ranging 1 to 70 years. Four out of seven fistulae closed within 21 days of starting the drug. One case, where fistula took over a month to close, responded well in reducing the output significantly within 10 days of starting therapy. The cases and the results are discussed. Favourable results following Octreotide therapy in this study need strengthening by further studies.

INTRODUCTION

Enterocutaneous fistula is a dangerous and challenging complication of abdominal surgery. The standard management is conservative. Surgery is reserved for complicated cases and those fistulae which refuse to close spontaneously^{1,2}. Both conservative and surgical management are associated with their specific complications leading to prolonged, uncomfortable and costly stay in the hospital.

Octreotide (Sandostatin), a long acting somatostatin analogue was introduced in the management of Enterocutaneous fistulae in the eighties and a number of trials^{3,4,5} have been conducted since then, reporting usefulness of the product, especially in reducing the spontaneous closure time of the fistulae. These reports aroused our interest to assess the efficacy of the drug in the management of Enterocutaneous fistulae.

MATERIALS AND METHODS

Seven consecutive cases of Enterocutaneous fistulae following abdominal surgery were observed for their output, local complications and closure of fistula. Fistulae were categorized according to Irving and

Beadle classification⁸. Octreotide therapy in a dose of $\mu\text{g}/\text{kg}$ body weight /24 hours was started subcutaneously from the 6th day onward of fistula formation except in one case where the index operation was carried elsewhere, in which case the drug was started on 14th post fistula day. Daily measurement of output in all the cases was recorded in addition to observation on thickness of the effluent. The improvement in the per-fistula skin and wound pathology was also noted. All patients were maintained on parenteral nutrition which was recorded in addition to general condition and daily weight measurement.

CASES

Patient 1: One-year-old male had manual reduction of acute ileo-colic intussusception on laparotomy. On 7th postoperative day he developed faecal fistula. By 12th day his fistula output had increased to 400 ml /24 hrs. Octreotide was started and his fistula was observed to be dry on 10th post treatment day.

Patient 2: 20 years old female had emergency laparotomy for enteric perforation which could not be properly dealt with at operation due to unstable condition of the patient and abdomen was closed after toilet. A high output faecal fistula developed on 5th post-operative day. Patient remained toxic and a second look operation was carried out on 9th post-operative day when a big subphrenic abscess was drained but nothing could be done for enteric fistula. Octreotide was started immediately after second operation. Her fistula closed on 9th day after the institution of Octreotide.

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Patient 3: 10 years old male underwent laparotomy in private hospital for intestinal obstruction due to ileal strictures (? Tuberculous). Stricturoplasty was done for one of the strictures which was considered as the cause of obstruction. Patient developed faecal fistula on 8th post-operative day. He was re-explored after a week and anastomotic leak was repaired. However, fistula persisted and patient was shifted to our unit for further management on 6th post fistula day. Approximately 300 ml fistulous output was measured /24 hrs and Sandostatin was started on tenth post fistulous day. Fistula became dry after 14 days of treatment.

Patient 4: 12 years old female underwent laparotomy which revealed plastic peritonitis due to tuberculosis (confirmed on omental biopsy). Enterocutaneous fistula developed on 7th postoperative day. Fistulous discharge was estimated to be more than 500 ml /day. Octreotide started on 4th post fistulous day. On 11th day of treatment fistulous output was measured as 80 ml and it persisted in the range of 50-100 ml for the next four days when patient left hospital against medical advice and was lost to follow up.

Patient 5: 19 years old male who had developed Enterocutaneous fistula through wound of entry five days after being stabbed. laparotomy revealed an ileal rent which was repaired after freshening its edges. On 9th post-operative day he developed a high output fistula and Sandostatin was started immediately. There was reduction of affluent from over 900 ml to 100 ml by 6th day. However, the effluent increased to 500 ml in the next six days. It was found that she was not getting the drug due to non-availability. She was started on drug again and her fistula was reported as dry on 21st day of treatment.

Patient 6: 36 years old female was operated for enteric perforation and had wedge resection and anastomosis at the site of perforation of the gut. She developed septicaemia post operatively and recovered. She developed a high output fistula on 6th post-operative day which was estimated to be 600 ml /24 hrs. Octreotide was started on 4th post fistulous day. She died on 11th day of the treatment due to second attack of septicaemia. Fistulous output was 60 ml on her last day of life.

Patient 7: 70 years old male operated for high rectal carcinoma which was adherent to small gut loops. The loops were freed from the tumour and anterior resection with transverse colostomy carried out. He developed faecal fistula on 5th post-operative day which was observed to be

small gut fistula due to consistency of its contents. Patient was started on Octreotide and his fistula was dry on tenth day.

RESULTS & CONCLUSIONS

Seven patients were included in the study with individual ages 1,9,12,19,20,30 and 70 years with a mean of 23 years. Three patients were males while two were females. Six patients had their index operation in the same unit while 7th patient was referral from elsewhere following abdominal surgery and fistula formation.

It is worthy to note that four out of seven cases had complete closure of fistulae within 12 days of the therapy while the 5th one reduced its output from 900 ml to 100 ml within seven days of the therapy; however, there was a rise in the output in the following 6 days mainly because there was no compliance of drug therapy due to non-availability of the drug. After the drug was re-instituted the output was reduced to nothing within further two weeks. The consistency of fluid output became thick and more mucinous in all the cases. Observation of peri-fistula pathology in 4 cases showed complete healing. In one of these cases, where the fistula opening was lying in the depth of wound dehiscence, the wound had to be resutured; the other two had moderate excoriation of skin at the time of departure from hospital.

DISCUSSION

Postoperative Enterocutaneous Fistula is a major surgical problem carrying significant morbidity and mortality. Its management is difficult, complex, lengthy and costly. Fluids and electrolyte imbalances should be rectified as soon as the condition is diagnosed. Elimination of sepsis, skin protection, bowel rest and nutritional support are the essential elements in management. The cure depends upon the anatomy and underlying disease as well^{2,3}. Surgery has an important role not only to deal with fistulae which refuse to heal by conservative management but also to eradicate sepsis. Septic foci should be dealt with as soon as they are diagnosed but definitive surgery during first six weeks is associated with high mortality and fistulous recurrence⁶. Most of the authors, therefore recommend conservative management during this early phase^{6, 7}. The requisite extensive nursing care, huge amount of fluid intake, expertise in stoma therapy and management are nutritional specially difficult to organize in developing countries like ours. The duration of the fistulae closure on conservative management has been tried to be reduced by

pharmacological means e.g. Cimetidine but increase in spontaneous closure rate could not be established.

Introduction of Somatostatin in this regards simplified the problem by speeding up the spontaneous closure time of Enterocutaneous fistulae. The effect of Somatostatin in gastrointestinal tract is to reduce the fistulous output on one hand and to increase the absorption of intestinal juice on the other hand. These pharmacological actions of somatostatin were well utilized to enhance the fistula closure by many authorities^{8,9}. However, short half-life of three minutes of the drug necessitated a continuous infusion with a steady rate which obviously posed a compliance problem. Octreotide is a long acting analogue of somatostatin with a half-life of over one hundred minutes. It is administrable by subcutaneous route, minutes following which peak concentration starts reducing⁹. A number of trials have been conducted on the effect of this drug in hastening fistula closure with favourable results i.e. up to 78 % closure rate in a mean of 4.5 days¹⁰⁻¹².

In our short study we achieved 70% rate within 21 days of treatment while rest of the cases had marked reduction in output. Parenteral nutrition given in our study is in accordance with some other authors^{13,14}. Sips of water allowed to the patient after 3 or 4 days following therapy did not increase the fistulous effluent.

REFERENCES

1. Aguire A, et al. The role of surgery and hyper-alimentation in therapy of gastrointestinal cutaneous fistulae. *Annals of Surg.* 1194, 180: 393-401.
2. Borison DI, et al. Treatment of Enterocutaneous and Colocutaneous fistulae with early surgery and Somatostatin analog. *Dis. Col. Rec.* 1992, 35: 635-8.
3. Boike GM. Treatment of small intestinal fistula with Octreotide, a Somatostatin analog. *J. Surg. Oncol.* 1992, 49: 444-5.
4. Dicastanzo J et al. Somatostatin in persistent gastrointestinal fistula treated by TPN. *Lancet* 1982, ii: 338-339.
5. El-Bahar T & Irving M. Intestinal Fistulas. *Recent Advances in Surgery*, 13, 1990; 103-124.
6. Hild P et al. Conservative treatment of fistulas of pancreas and small intestine with Somatostatin. *Ann. Chir.* 1982, 3: 193-196.
7. Harris GA. The role of Somatostatin and Somatostatin analogs in the management of gastrointestinal disease. *Current Medical Literature*, 1993: 40-42, London.
8. Irving M & Beadle C. External Intestinal Fistulas. *Clinics in Gastroenterology*, 11: 327-336.
9. Kovacs HA, et al. Treatment of a chronic Gastrocutaneous fistula with Octreotide in a pediatric patient. 1992; 15: A112 (Abs.685)
10. Nabiola-Calong P, et al. Blind evaluation of the efficacy of Octreotide, a Somatostatin analog, on small bowel fistula output. *Lancet*, 1987; 2: 672-3.
11. Nabiola P, et al. Treatment of 27 Enterocutaneous fistulas with a half-life Somatostatin analog (SMS 201-995). *Ann. Surg.* 1989, 210: 56-58.
12. Ray-Jade C, et al. Octreotide in the management of post-operative Enterocutaneous fistulas and stress ulcer bleeding. *Am. J. Gastroenterol.* 1992, 87: 1212-1215.
13. Sbanbhogue LKR, et al. Parenteral nutrition in the surgical patient. *Br. J. Surg.* 1987, 74: 172-180.
14. Zera RT, et al. Enterocutaneous fistulas. Effect of TPN and surgery. *Dis. Col. Rec.* 1983, 26: 109-112.