Treatment of High-output Gastric Fistulas with Omeprazole.

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Running head : Gastrocutaneous Fistulas.

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Summary

Two patients with high-output gastrocutaneous fistulas were treated with total parenteral nutrition and gastric antisecretory drugs. IV administration of omeprazole decreased in a rapid and significant way acid output in one patient, resulting in a spontaneous healing of the fistula after eight days of treatment. In the second patient omeprazole caused a marked inhibition of acidity of the fistula fluid which also closed without surgical operation. The longstanding decreased acid output induced by intravenous omeprazole may be much useful for promoting spontaneous closure of high-output gastrocutaneous fistula.

Keywords

Gastric fistula-Intestinal fistula-Omeprazole Parenteral feeding-Parenteral hyperalimentation.

Introduction

The incidence of isolated gastrocutaneous fistula in large series of gastrointestinal tract fistulas ranges between 3 and 10% (Table 1).

Gastric fistulas are described after splenectomy (1), highly selective vagotomy (2), anterior gastropexy (3) or gastrojejunal anastomosis (4). Other causes include perforated gastric ulcer, pancreatic abscess- or carcinoma, gunshot wounds (5) and radiation therapy (6).

The basic principles of treatment of these fistulas include: - adequate drainage and control of sepsis,
- reduction in acidity and volume of fluid loss,
- prevention of malnutrition.

Two patients with high-output gastrocutaneous fistulas are reported. As far as we know intravenous omeprazole has never been proposed in the treatment of gastrocutaneous fistula.

Patients

Case 1

A 49-year-old man was admitted with a stab wound in the ninth intercostal space at the right side. An emergency laparotomy was carried out and a laceration of the diaphragm, a transfixing wound of the right liver lobe and a perforation of the anterior wall of the second part of the duodenum were sutured and the right infrahepatic space was drained. By the sixteenth postoperative day he became jaundiced and septic with fever (39°C) and an elevated leucocyte cell count. CT scanning showed a sub-hepatic abscess with compression of the common bile duct. The

abscess was drained and a cholecystectomy was carried out. Total parenteral nutrition was started after the second operation. An upper gastrointestinal haemorrhage due to a gastric ulcer, as shown by endoscopy, occurred on the fifth day after the second operation at 3 weeks after trauma. The patient was given ranitidine (400 mg/day IV) but slow bleeding persisted. On the twenty-sixth day after admission the patient had to be reoperated for total abdominal wound dehiscence. During the same operation a gastrotomy was performed and a bleeding gastric ulcer was undersewn.

On the 33rd day the patient had a second evisceration. At laparotomy recurrent infrahepatic abscess extending to the right flank, a complete disruption of the former gastrotomy and a fistula of the sigmoid colon were found. A Hartmann's resection of the sigmoid colon with an end- colostomy was performed and the gastric opening was sutured again. The abdominal cavity was left open and daily peritoneal irrigations were carried out. The patient's general condition improved, but an important gastrocutaneous fistula appeared with an output ranging from 2 to 3 liters a day, despite the administration of high-doses of cimetidine (1600 mg/day IV) (Fig.1). Addition of pirenzepine (30 mg/day IV) did not decrease the fistula output, whereas the pH of the fluid collected from the fistula varied between 2,5 and 4. Parenteral nutrition was replaced by enteral nutrition, administered through a jejunostomy on the 94th day. On the 114th day post-trauma antisecretory drugs were stopped during 24 hours and a 11,2 mEq H^+/hour acid output via the fistula was measured. Administration of cimetidine (1600 mg/day IV) decreased the acid output to 5 mEq H^+/hour. A similar effect was obtained with

ranitidine (600 mg/day IV). On the 117th day intravenous omeprazole was started at an initial doses of 80 mg/day during 3 days and then 20 mg/day from day 4. The fistula output decreased from 1500 ml/day to less than 100 ml/day after 3 days of omeprazole treatment (fig.1). At the same time acid output decreased to 1,7 mEq H^+/hour. After 8 days of treatment with omeprazole the gastric fistula closed spontaneously. The patient could be given an oral diet from two days later.

Case 2

A 48-year-old man was admitted after a car accident. This obese patient had a fracture of the left clavicula and of the two distal ribs, a lungcontusion and a left-sided hemothorax, a fracture of the left ulna, a luxation of the head of the radius a fracture of the left femur and an important hemo-peritoneum. After rescuecitation an emergency laparotomy was carried out. Mesenteric lacerations and a ruptured spleen requiring splenectomy were found. On the next day the patient had to be reoperated for continuous blood loss from the left abdominal drain and a distal pancreatectomy was carried out for bleeding pancreatic lacerations. A pancreatic fistula with an output of less than 200 ml/day appeared on the sixth day after the latter laparotomy. Eight days after admission the fractures of the left ulna and femur were stabilised by osteosynthesis. Artificial ventilation and intubation had to be maintained until day 12. At this time, the patient developed acute abdominal symptoms. At operation a large perforation was found high on the greater curvature of the stomach. The opening was sutured and the left subphrenic space was drained. TPN was started but the patient

became septic and had to be reoperated on day 24 via a left subcostal incision for a subphrenic abscess. Besides the abscess, two important openings along the greater curvature of the fundic part of the stomach were found. As it was impossible to close the gastric wall defects without major resection, 2 Foley catheters were inserted and brought out as gastrostomies. The left subphrenic space was extensively drained, a nasogastric aspiration was maintained and ranitidine (200 mg/day) was administered intravenously. From this moment the patient's general condition improved neatly but the daily fistula output varied between 400 and 500 ml with a pH ranging between 3 and 5 and TPN was still required. Ranitidine was replaced by I.V. omeprazole (2 x 40 mg/day) on the 32nd day. pH of the collected fistula fluid was monitored four times a day: 71% of the pH values were above 6 during omeprazole treatment (fig. 2). Both Foley catheters and subphrenic drains were progressively removed. Upper GI series performed on the 49th day showed a narrowing gastrocutaneous tract. On the 17th day of I.V. omeprazole treatment the patient complained of itching which disappeared by stopping this treatment. Complete closure of the fistula was obtained 4 days later. From that time the patient resumed a normal diet and the TPN was stopped. The patient was discharged from the hospital on day 63.

Discussion

As most gastrocutaneous fistulas occur postoperatively with intra-abdominal abscess formation, adequate drainage of the abscess and fistula is the first priority (5,7). Uncontrolled sepsis is the major determinant of mortality and will render the nutritional support and other parasurgical care

ineffective (7). Both our patients underwent several operations to evacuate intraabdominal abscesses and to drain the gastric fistulas. The gastric fistula of the first patient was located in the distal part of the stomach which contributed to the high fluid losses and acid output. The fistulas of the second patient were located in the proximal stomach, thus explaining the relatively lower output.

The introduction of total parenteral nutrition in the treatment of gastrointestinal fistulas has been associated with an increased rate of spontaneous closure (7,8,9,10). The benefits of intravenous hyperalimentation in the management of gut fistulas were related to the secretory and mechanical bowel rest as well as to the restoration of a normal nutritional status (8). The effect of TPN on gastric secretion in humans is not well documented. We know that acute intravenous administration of a mixture of L-amino acids causes a significant increase in gastric acid secretion which can be inhibited by intravenous fat (Intralipid°) administration (11,12,13,14). We could not find any report on the effect of longterm TPN on gastric secretion in humans but we know that large fluid losses (1500-2500 ml/day) from gastric or duodenal fistulas can persist in patients receiving TPN only (15).

Gastric antisecretory drugs can reduce fluid losses in gastric fistula patients. The combined treatment of TPN and somatostatin has resulted in an important fistula output reduction and in early closure of gastrointestinal fistulas (16). However, withdrawal of somatostatin may be followed by a rebound phenomenon (17). The H_2- receptor antagonist cimetidine has been proposed used in decreasing proximal intestinal fistula output (15,18). We observed a 55 per cent decrease in acid output with IV cimetidine

and with ranitidine in our first patient. However, large fluid losses persisted despite this significant reduction in acid output and addition of pirenzepine to H_2-blockers had little effect.

Omeprazole inhibits the enzyme H^+/K^+ATPase, which is the final step of gastric acid secretion (19). Its inhibitory effect is thus not dependent on the mode of stimulation of the acid secretion (20). IV administered omeprazole in doses ranging from 10 to 80 mg dose dependently inhibits pentagastrin stimulated acid secretion with an almost complete inhibition at 80 mg (21). Moreover the gastric secretion of pepsin is also decreased by omeprazole (22).

The dramatic effect of IV omeprazole on acid secretion was well documented in the first patient : a 85% decrease in acid output and a reduction in fistula output of more than 90% was obtained after starting omeprazole. This reduction in gastric secretion was followed by complete fistula closure after 8 days of IV omeprazole treatment. In the second patient 71% of pH measurements during the IV omeprazole treatment period were above 6, a pH at which pepsin is irreversibly degraded (23). Nearly all pH measurements during IV cimetidine and ranitidine were below 6.

In conclusion, IV omeprazole has provided a nearly total gastric achlorhydria which resulted in spontaneous closure of the fistulas in two patients with high-output gastric fistulas. Further reports will be necessary to confirm the beneficial effect of this drug for such patients.

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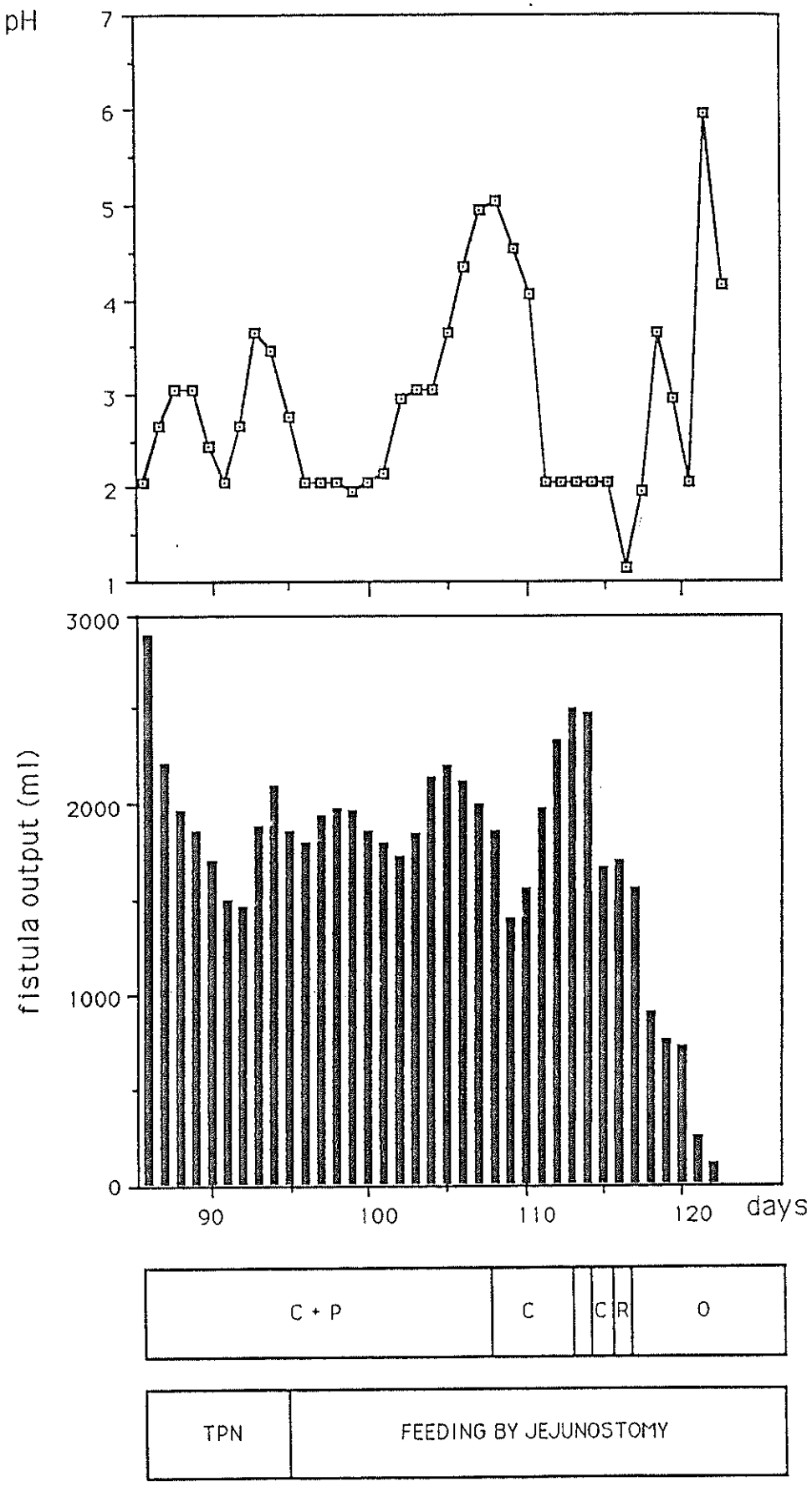
Table 1 : Incidence of isolated gastrocutaneous fistulas in large reviews of gastrointestinal tract fistulas.

Author			Incidence	Percentage (%)
MacFadyen	(9)	(1973)	6/ 61	9.8
Aguirre	(24)	(1974)	3/ 38	7.9
Deitel	(25)	(1976)	6/100	6
Reber	(15)	(1978)	14/186	7.5
Soeters	(7)	(1979)	4/119	3.4
Rose	(10)	(1986)	6/114	5.3
Di Costanzo	(16)	(1987)	2/ 37	5.4

LEGEND OF FIGURES

Fig. 1 Evolution of fistula output and pH of the daily collected fistula fluid during different anti- secretory therapy in the first patient. C + P : cimetidine 1600 mg/d + pirenzepine 30 mg/d;
C : cimetidine 1600 mg/d; R : ranitidine 600 mg/d; O : omeprazole 20 mg/d; TPN : total parenteral nutrition.

Fig. 2 Daily fistula output (▬) and nasogastric aspirated volume (▭) during different antisecre- tory therapy in the second patient. Each point of the pH curve represents the mean of four pH measu- rements daily. C : cimetidine 1200 mg/d;
R : ranitidine 200 mg/d; O : omeprazole 80 mg/d; TPN : total parenteral nutrition.


pH
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4
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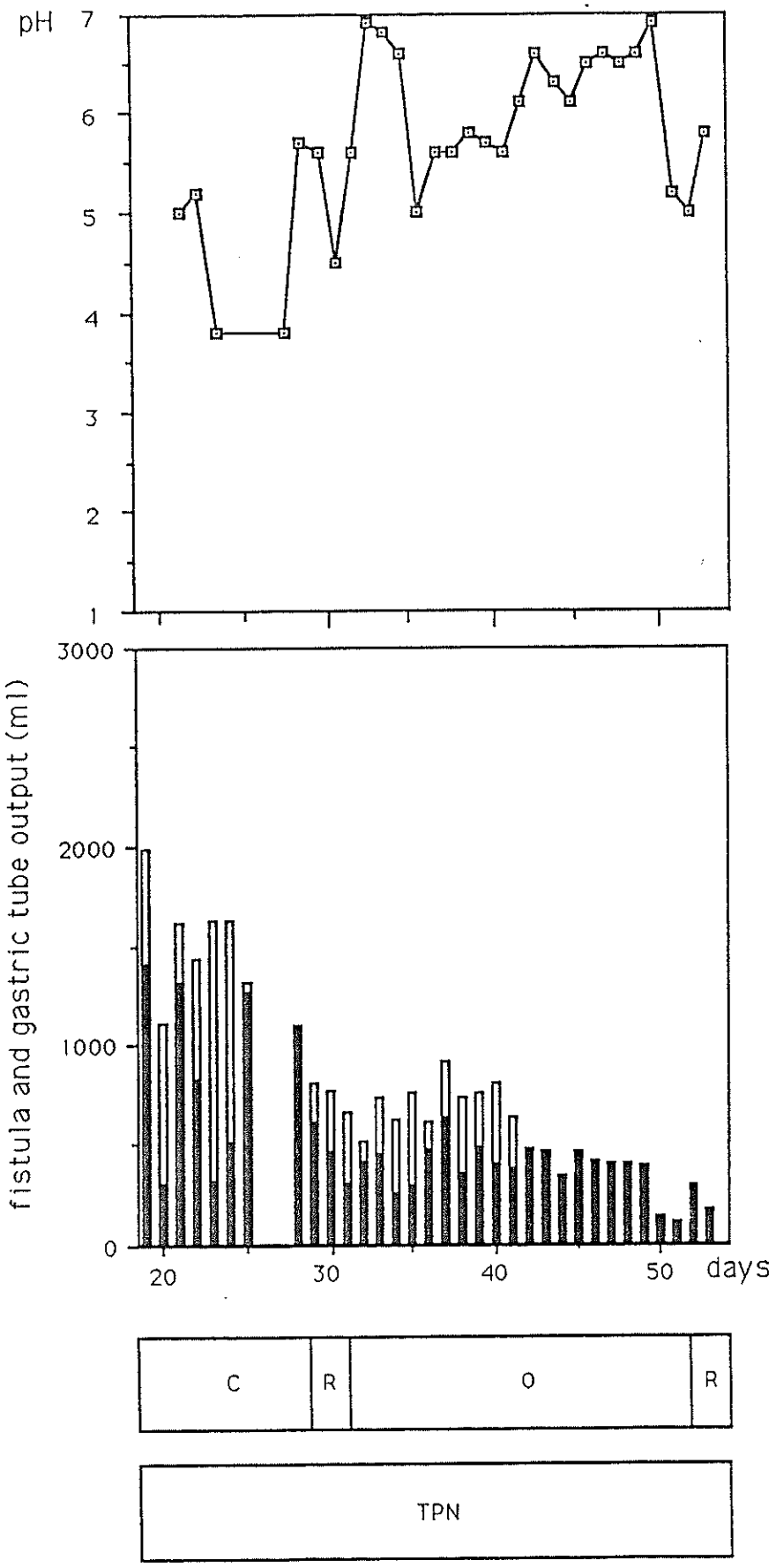
pH
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Professor Gerard Willems
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Amsterdam, July 10, 1989
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Dear Professor Willems,

I am most pleased to let you know that your manuscript entitled "Treatment of High-output Gastric Fistulas with Omeprazole" (our number M 89158) has been accepted for publication in the journal Hepato-Gastroenterology. I think that your study might offer a solution to a controversial and challenging item.

On this occasion I would like to invite you for the first meeting of the International Gastro-Surgical Club, which is held this year in Amsterdam. For further details you can contact Professor Rubens or Professor Kloeppel.
I would be most pleased to have you here with me so that we can discuss the future prospectives for our club. I think that the meeting will be fantastic. We expect more than 300 participants from more than 37 countries.

Looking forward to hearing from you,
With best regards,
Sincerely yours,

p/a Elisabeth Gleveld

Prof. Agr. N.J. Lygidakis

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