Original Article

Role of Octreotide, Scopolamine Butylbromide, and Hydration in Symptom Control of Patients with Inoperable Bowel Obstruction and Nasogastric Tubes: A Prospective Randomized Trial

Carla Ripamonti, MD, Sebastiano Mercadante, MD, Liliana Groff, MD, Ernesto Zecca, MD, Franco De Conno, MD, and Alessandra Casuccio, MD

Pain Therapy and Palliative Care Division (C.R., L.G., E.Z., F.D.), National Cancer Institute, Milan; Pain Relief and Palliative Care Unit (S.M.), S.A.M.O.T., Palermo; and Department of Hygiene and Microbiology (A.C.), University of Palermo, Palermo, Italy

Abstract

Bowel obstruction may be an inoperable complication in patients with end-stage cancer. Scopolamine butylbromide (SB) and octreotide (OCT) have been successfully used with the aim of reducing gastrointestinal (GI) secretions to avoid placement of a nasogastric tube (NGT); however, there have been no comparative studies concerning the efficacy of these drugs. Furthermore, there is little information about the role played by parenteral hydration in symptom control of these patients. In a prospective trial that involved all 17 inoperable bowel-obstructed patients presenting to our services with a decompressive NGT, patients were randomized to OCT 0.3 mg/day or SB 60 mg/day for 3 days through a continuous subcutaneous infusion. Clinical data, survival time, and the time interval from the first diagnosis of cancer to the onset of inoperable bowel obstruction were noted. The intensity of pain, nausea, dry mouth, thirst, dyspnea, feeling of abdominal distension, and drowsiness were assessed by means of a verbal scale before starting treatment with the drugs under study (T0) and then daily for 3 days (T1, T2, T3). Moreover, daily information was collected regarding the quantity of GI secretions through the NGT, the oral intake of fluids, the quantity of parenteral hydration, and the analgesic therapy used. The NGT could be removed in all 10 home care and in 3 hospitalized patients without changing the dosage of the drugs. OCT significantly reduced the amount of GI secretions at T2 (P = 0.016) and T3 (P = 0.020). Compared to the home care patients, the hospitalized patients received significantly more parenteral hydration (P = 0.0005) and drank more fluids (P = 0.025). There was no difference in the daily thirst and dry mouth intensity in relation to the amount of parenteral hydration or the treatment provided (OCT or SB). Independent of antisecretory treatment, the patients receiving less parenteral hydration presented significantly more nausea (T0 P = 0.002; 0.025; 0.016).
T1 P = 0.001; T2 P = 0.003; T3 P = 0.001) and drowsiness at T3 (P < 0.05). Pain relief was obtained in all 17 patients and only two patients required an increase in the morphine dose at T1. All patients with inoperable malignant bowel obstruction should undergo treatment with antisecretory drugs so as to evaluate the possibility of removing the NGT. When a more rapid reduction in GI secretions is desired, OCT should be considered as the first choice drug. Parenteral hydration over 500 ml/day may reduce nausea and drowsiness. J Pain Symptom Manage 2000;19:23–34. © U.S. Cancer Pain Relief Committee, 2000

**Key Words**
Octreotide, scopolamine butylbromide, hydration, cancer, bowel obstruction

**Introduction**

Bowel obstruction is a common complication in patients with end-stage cancer, particularly in those with an abdominal or pelvic primary.1-3 Not all patients are suitable candidates for surgery. The rate of inoperable patients ranges from 6% to 50%.2 Moreover, in cancer patients with bowel obstruction, the rate of operative mortality (defined as death from any cause within 30 days of the operation) ranges from 30% to 40%, and complication rates vary from 27% to 90%.2, 4-6 Hence, the physician has to deal with a patient suffering from vomiting and pain, with a short life expectancy, who can only be treated with palliative medical therapies.

The usual hospital treatment for control of the symptoms is nasogastric suction and liquid supplementation. This is useful in treating decompression of the stomach or intestine, for correcting fluid and electrolyte imbalance before surgery, or while awaiting a decision on other therapy. Prolonged nasogastric suction for symptomatic treatment of inoperable patients is not recommended. This treatment can create complications and discomfort in patients who are already distressed by previous anticancer and surgical therapies.

Drug treatment (analgesics, antiemetics, and antisecretory drugs) without a nasogastric tube (NGT) is successful in most patients, and particularly in those with large bowel occlusion, and can be employed in both inpatient and outpatient settings.7-19 To reduce gastrointestinal (GI) secretions, two classes of antisecretory drugs are used: anticholinergics, such as scopolamine butylbromide (SB),2,7,9,18 and somatostatin analogues, such as octreotide (OCT)12-15,19 and, less frequently, vaprotide.16 The two drugs act with different mechanisms of action. The anticholinergic activity of SB decreases the tonus and peristalsis in smooth muscle, both by competitive inhibition of muscarinic receptors at the smooth muscle level and by impairment of ganglionic neural transmission in the bowel wall.20,21 Muscarinic cholinergic receptors have also been observed on mucosal cells of the intestinal lumen and in human salivary glands,22,23 which explains its ability to reduce intestinal secretions.9,18 OCT modulates gastrointestinal function by reducing gastric acid secretion, slowing intestinal motility, decreasing bile flow, increasing mucus production, and reducing splanchnic blood flow.15,24,25 Its inhibitory effect causes a decrease in water and sodium secretion of the intestinal epithelium, and thereby reduces distension of the bowel.

There have been no comparative studies concerning the efficacy of SB and OCT in reducing symptoms and GI secretions in bowel-obstructed patients. Furthermore, there is little information about the role played by parenteral hydration in symptom control of these patients. The aims of our study were (1) to compare the GI antisecretory effect of OCT versus SB in patients with an NGT due to inoperable malignant bowel obstruction; (2) to evaluate in how many patients and after how long the NGT could be removed; and (3) to evaluate the effect of intravenous hydration in symptom control, particularly in relieving thirst, dry mouth, nausea, drowsiness, and the feeling of abdominal distension.

**Methods**

**Subjects**

In a prospective, randomized clinical trial, we considered all the patients presenting to us with a decompressive NGT and a clinical and/or radiological and/or surgical diagnosis of inoperable bowel obstruction in whom available oncologic therapies for tumor control had
been exhausted. The following were excluded: (1) patients having already undergone treatment with the drugs under study; (2) patients with obstruction at the duodenal level, in whom removal of the NGT is difficult; (3) patients with cognitive failure; (4) uncooperative patients; and (5) patients not giving their informed consent to participate in the study.

The study was carried out by the Pain Therapy and Palliative Care physicians of the National Cancer Institute of Milan and the Pain Relief and Palliative Care physicians of Palermo (SAMOT) from September 1995 to September 1997.

Care Setting
The Milan patients were admitted to the Oncological Surgery Divisions of the National Cancer Institute of Milan. In these Divisions, we had the role of pain therapy consultants and were asked to see to the palliative treatment of symptoms without modifying other treatments, such as the type and quantity of the parenteral hydration administered to the patients. The Palermo patients were followed at home by means of a palliative home care team having total management of the patient.

Data Collection
Evaluation of the patients was carried out via a specific assessment instrument that included: age, gender, Eastern Cooperative Oncology Group (ECOG) performance status score, care setting, primary/secondary tumor site, therapies carried out for cancer (surgery, chemotherapy, radiotherapy, others), number of days with NGT before starting administration of antisecretory drugs, previous episodes of bowel obstruction and relative therapies, the criteria used to define the patient as being unsuitable for surgery, and who made the decision to forego surgery. Whenever possible, we collected the patient’s present status of bowel obstruction: diagnosis (clinical, radiological, surgical), type (partial, complete, mechanical, paralytic, single, multiple), and level (small bowel, large bowel, or both). The data regarding the time interval from the first diagnosis of cancer and the onset of inoperable bowel obstruction were recorded, as well as the data on survival time starting from the beginning of the study (T0).

The intensity of the following symptoms was evaluated: continuous and colicky pain, nausea, dry mouth, thirst, dyspnea, feeling of abdominal distention, and drowsiness. All symptoms were assessed through a verbal rating scale with four possible answers: 0 = not at all, 1 = slight, 2 = a lot, and 3 = awful. All the symptoms were assessed before starting treatment with the drugs under study (T0) and then daily for 3 days (T1, T2, T3). Each daily assessment referred back to the previous 24 hours. Moreover, we recorded the daily quantity of GI secretions through the NGT, the oral intake of water, the amount of parenteral hydration through the intravenous (IV) or subcutaneous (SC) routes, and the analgesic therapy administered.

Treatments
Patients were assigned to OCT treatment or SB alternately after the random selection of therapy for the first patient. The patients were to receive the following treatments: OCT (Novartis Farma, Origgio, Varese, Italy) 0.3 mg/daily for 3 days or SB (Boehringer Ingelheim Italia, Firenze, Italy) 60 mg/daily for 3 days. These dosages were extrapolated by previous experience which indicated that the OCT effective dose range is 0.2 to 0.9 mg/day and the effective dose range of SB is 40 to 120 mg/day.

Drugs were administered by a continuous subcutaneous infusion by means of a syringe driver. Pain therapy was carried out concurrently according to the World Health Organization (WHO) guidelines. The dosage of analgesic could be increased and/or the type of analgesic could be changed until pain relief was achieved. From T0 to T3, the patients were not given steroids, antiemetics, anticholinergics, H2 blockers, or omeprazole.

The data were analyzed only for the 3-day study period. After 3 days, each researcher was free to change to the alternate drug, to administer SB and OCT in association, to carry on with the same treatment if it proved efficacious, to increase the dosages of the drugs, to leave the NGT attached, or to remove it.

Data Analysis
Pearson chi-square test was used to evaluate the differences of age, gender, and primary tumors in the Palermo and Milan patients. One-way analysis of variance (ANOVA) was used to assess the differences of ECOG performance status and patient survival between the two centers. Data were analyzed using the Mann-Whit-
ney U test to compare differences between the patients of Milan and Palermo and the differences between the two treatments, OCT/SB (i.e., to compare a single variable across two independent groups). The Wilcoxon signed-ranks test was used to compare the data at different times. Patients with missing data for an item were eliminated from the analysis for that item. Differences resulting in \( P \) values less than 0.05 were considered statistically significant.

**Results**

Table 1 reports the patients’ characteristics, oncological therapies, the number of days with NGT before beginning treatment (T0), and the antisecretory drug used. There were 11 female and 6 male patients with a mean age of 61.23 ± SD 9.0 (range 45–75 years). All the patients presented with abdominal or pelvic primary tumors with metastases and/or relapse.

The 17 patients had all undergone oncological treatment previously. Eight patients received SB (3 in Milan and 5 in Palermo) and 9 received OCT (4 in Milan and 5 in Palermo). The mean survival time in all the patients starting from T0 was 11.6 ± SD 4.0 (range 4–17 days). There was no statistically significant difference between the hospitalized group and the home care group regarding age, gender, primary tumors, and ECOG at T0 and survival.

Tables 2 and 3 show the data regarding both the previous as well as the actual bowel obstruction of the patients and the time interval from the beginning of the study and the day of death and the day at which the NGT could be removed, if possible. Seven patients had a previous episode of bowel obstruction relieved from T0 was 3–8 days; respectively, before symptoms of obstruction reemerged. With regard to the present bowel obstruction, surgical intervention was judged as useless by one or more doctors because the patients presented poor prognostic factors for surgical benefit according to the data in the literature.\(^2\) One patient refused surgery because he was aware of the progressive malignancy and desired no further invasive interventional. The type of obstructions was mechanical, with or without intraperitoneal carcinomatosis. Occlusion occurred at small bowel, large bowel, or both. The mean time interval from the first diagnosis of cancer and the onset of inoperable bowel obstruction was 13.1 ± 6.4 months (range 6–24 months).

The hospitalized patients received a significantly higher quantity of IV fluids daily (≥ 2000 ml) than the home care patients (≤500 ml through the SC route) at all the considered times, with a significant difference at T1 (\( P = 0.001 \)), T2 (\( P = 0.0005 \)), and T3 (\( P = 0.0005 \)). Furthermore, the hospitalized patients drank more fluids (250 to 1000 ml/day) from T0 to T3 (\( P = 0.025 \)). The home care patients drank from 100 to 250 ml/day at a constant daily quantity for each patient. For the hospitalized patients, we did not know how much liquid was absorbed and how much was discharged into the bag connected to the NGT. For this reason, we considered trends in the quantity of NGT secretions in all the 17 patients, but compared the efficacy between the two antisecretory drugs using only the 10 Palermo home care patients who drank a constant amount of liquids daily. In all the 17 patients, there was a significant reduction in the secretions at T1 vs. T2 (\( P = 0.044 \)) and T1 vs. T3 (\( P = 0.040 \)), independently of the treatment OCT/SB. In the 10 Palermo patients, the reduction of the NGT secretions was significant at T0 vs. T2 (\( P = 0.005 \)); T0 vs. T3 (\( P = 0.008 \)); T1 vs. T2 (\( P = 0.005 \)); and T1 vs. T3 (\( P = 0.008 \)).

Figure 1 shows a comparison of the amount of NGT secretions at T0 in the Palermo patients treated with OCT (5 patients) and those treated with SB (5 patients). There was a significant secretion reduction in the patients treated with OCT at T2 (\( P = 0.016 \)), 95% CI 319.5–950.5) and at T3 (\( P = 0.020 \), 95% CI 298.2–861.7). The same figure shows the significant reductions of the secretions between the different assessment times with both drugs.

In the home care patients treated with OCT, it was possible to remove the NGT from 3 to 5 days after T0. In those treated with SB, the NGT could be removed from 3 to 8 days after T0 (mean 4.9 ± SD 1.66; range 3–8 days; \( P = 0.287 \) (Table 3). In Milan-hospitalized patients (Table 2), the NGT was removed in 3 patients 1 day (2 patients) and 2 days (1 patient) respectively after the end of
In the study period (2 with OCT and 1 with SB); 1 patient on OCT died with the NGT in hospital the day after the end of the study. In the other patient treated with OCT, the NGT was removed when the dose of the drug was doubled. In 1 patient treated with SB, the NGT was removed after being discharged from the hospital when the IV hydration was reduced from 2000 ml/day to 500 ml/day and the dose of SB was doubled. In another patient, it was possible to remove the NGT when OCT was added to SB for 2 days after the end of the study.

Table 4 shows the mean daily intensity and the significant reductions between the different assessment times of the continuous pain and colicky pain in all 17 patients, 8 patients on SB, and in 9 patients treated with OCT. At T0, a statistically significant reduction was observed, both in the case of continuous as well as colicky pain in patients treated with OCT and those treated with SB (the P was evaluated between assessment times through the Mann-Whitney test). No significant difference in continuous and colicky pain between the OCT group and the SB group was observed at the assessment times.

No difference in pain relief was observed between the home care and the hospitalized groups and there were no differences in the types and dosages of analgesic drugs. All the

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age, gender</th>
<th>ECOG</th>
<th>City</th>
<th>Primary tumor</th>
<th>Metastasis, relapse</th>
<th>Oncological therapies</th>
<th>No. days with NGT at T0</th>
<th>Antisecretory drugs therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 QL</td>
<td>61 F</td>
<td>3</td>
<td>M</td>
<td>Ovary</td>
<td>Liver, abdomen, pleural effusion</td>
<td>SURG, CHT</td>
<td>12</td>
<td>OCT</td>
</tr>
<tr>
<td>2 PM</td>
<td>48 F</td>
<td>4</td>
<td>M</td>
<td>Breast, ovary, endometric</td>
<td>Omentum, ovary relapse</td>
<td>SURG, CHT</td>
<td>4</td>
<td>OCT</td>
</tr>
<tr>
<td>3 CA</td>
<td>62 F</td>
<td>4</td>
<td>M</td>
<td>Cholecyst</td>
<td>Liver</td>
<td>SURG, CHT, biliary drainage</td>
<td>2</td>
<td>OCT</td>
</tr>
<tr>
<td>4 CF</td>
<td>67 M</td>
<td>4</td>
<td>M</td>
<td>Colon</td>
<td>Liver, abdominal lymph nodes</td>
<td>SURG, CHT</td>
<td>12</td>
<td>OCT</td>
</tr>
<tr>
<td>5 CA</td>
<td>61 F</td>
<td>4</td>
<td>M</td>
<td>Ovary</td>
<td>Liver, omentum</td>
<td>SURG, CHT</td>
<td>4</td>
<td>SB</td>
</tr>
<tr>
<td>6 CC</td>
<td>75 F</td>
<td>4</td>
<td>M</td>
<td>Ovary</td>
<td>Liver</td>
<td>SURG, CHT</td>
<td>1</td>
<td>SB</td>
</tr>
<tr>
<td>7 HM</td>
<td>48 F</td>
<td>4</td>
<td>M</td>
<td>Ovary</td>
<td>Omentum</td>
<td>SURG, CHT, RT</td>
<td>1</td>
<td>SB</td>
</tr>
<tr>
<td>8 PC</td>
<td>72 M</td>
<td>3</td>
<td>P</td>
<td>Colon–rectum</td>
<td>Bones, pleural effusion</td>
<td>SURG, CHT</td>
<td>3</td>
<td>OCT</td>
</tr>
<tr>
<td>9 AC</td>
<td>65 M</td>
<td>4</td>
<td>P</td>
<td>Stomach</td>
<td>Liver, omentum</td>
<td>SURG</td>
<td>12</td>
<td>OCT</td>
</tr>
<tr>
<td>10 GF</td>
<td>58 F</td>
<td>4</td>
<td>P</td>
<td>Ovary</td>
<td>Ovaric relapse, abdominal diffusion</td>
<td>SURG, CHT, RT</td>
<td>4</td>
<td>OCT</td>
</tr>
<tr>
<td>11 CR</td>
<td>63 M</td>
<td>4</td>
<td>P</td>
<td>Pancreas</td>
<td>Peritoneum, Liver, peritoneum</td>
<td>SURG, CHT</td>
<td>2</td>
<td>OCT</td>
</tr>
<tr>
<td>12 FT</td>
<td>55 F</td>
<td>4</td>
<td>P</td>
<td>Ovary</td>
<td>Peritoneum, Liver, colon relapse</td>
<td>SURG, CHT</td>
<td>2</td>
<td>OCT</td>
</tr>
<tr>
<td>13 PC</td>
<td>72 M</td>
<td>4</td>
<td>P</td>
<td>Colon–rectum</td>
<td>Peritoneum, Ovaric relapse</td>
<td>SURG, CHT</td>
<td>1</td>
<td>SB</td>
</tr>
<tr>
<td>14 AS</td>
<td>61 F</td>
<td>4</td>
<td>P</td>
<td>Pancreas</td>
<td>Peritoneum, Liver, ovary relapse</td>
<td>SURG, CHT</td>
<td>6</td>
<td>SB</td>
</tr>
<tr>
<td>15 FD</td>
<td>73 F</td>
<td>4</td>
<td>P</td>
<td>Ovary</td>
<td>Peritoneum, Liver, omentum</td>
<td>SURG, CHT</td>
<td>1</td>
<td>SB</td>
</tr>
<tr>
<td>16 GD</td>
<td>55 F</td>
<td>4</td>
<td>P</td>
<td>Ovary</td>
<td>Peritoneum, Liver, omentum</td>
<td>SURG, CHT</td>
<td>4</td>
<td>SB</td>
</tr>
<tr>
<td>17 LC</td>
<td>45 M</td>
<td>4</td>
<td>P</td>
<td>Stomach</td>
<td>Peritoneum, Liver, omentum</td>
<td>SURG, CHT</td>
<td>3</td>
<td>SB</td>
</tr>
</tbody>
</table>

City: M, Milan; P, Palermo. SURG, surgery; CHT, chemotherapy; RT, radiotherapy; OCT, octreotide; SB, scopolamine butylbromide.
### Table 2
Data Regarding the Previous and Present Bowel Obstruction in Milan Patients

<table>
<thead>
<tr>
<th>Patients</th>
<th>Previous episodes of bowel obstruction</th>
<th>Diagnosis present obstruction</th>
<th>Criteria of inoperability</th>
<th>Doctors involved in the decision not to operate</th>
<th>Type of obstruction/level of obstruction</th>
<th>NGT removal</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 QL</td>
<td>None</td>
<td>Surgical (exploratory laparotomy)</td>
<td>Technically impossible for the adhesion of the tumor to the abdomen wall, peritoneal carcinomatosis</td>
<td>Surgeon</td>
<td>Mechanical + peritoneal carcinomatosis/Small and large bowel</td>
<td>Yes, when OCT dose was doubled</td>
<td>5*</td>
</tr>
<tr>
<td>2 PM</td>
<td>Intestinal bypass, therapy with taxol 1 month before</td>
<td>Clinical + radiological</td>
<td>Poor PS, ovarian relapse, previous intestinal bypass</td>
<td>Surgeon</td>
<td>Mechanical + peritoneal carcinomatosis</td>
<td>Yes, 4*</td>
<td>4*</td>
</tr>
<tr>
<td>3 CA</td>
<td>None</td>
<td>Clinical + radiological</td>
<td>Poor PS, multiple sites of obstruction, peritoneal carcinomatosis</td>
<td>Surgeon</td>
<td>Mechanical + peritoneal carcinomatosis</td>
<td>—</td>
<td>13*</td>
</tr>
<tr>
<td>4 CF</td>
<td>None</td>
<td>Clinical + radiological</td>
<td>Poor PS, multiple sites of obstruction, cachexia</td>
<td>Surgeon, oncologist, PC doctor</td>
<td>Mechanical/smaller and large bowel</td>
<td>Died the day after the end of the study with the NGT</td>
<td>7*</td>
</tr>
<tr>
<td>5 CA</td>
<td>None</td>
<td>Clinical + radiological</td>
<td>Poor PS, omentum diffusion</td>
<td>Surgeon, PC doctor</td>
<td>Mechanical + peritoneal carcinomatosis</td>
<td>—</td>
<td>7*</td>
</tr>
<tr>
<td>6 CC</td>
<td>None</td>
<td>Clinical + radiological</td>
<td>Poor PS, severe liver involvement</td>
<td>Surgeon, oncologist</td>
<td>Mechanical/smaller and large bowel</td>
<td>Yes, when OTC was added to SB</td>
<td>8*</td>
</tr>
<tr>
<td>7 HM</td>
<td>None</td>
<td>Clinical + radiological</td>
<td>Peritoneal carcinomatosis, severe thrombopenia, poor PS</td>
<td>Surgeon, oncologist</td>
<td>Mechanical + peritoneal carcinomatosis/small bowel</td>
<td>Yes, 5*</td>
<td>10*</td>
</tr>
</tbody>
</table>

PC = palliative care; PS = performance status.

*Number of days from T0.

†Number of days before death.
### Table 3
Data Regarding the Previous and Present Bowel Obstruction in Palermo Patients

<table>
<thead>
<tr>
<th>Patients</th>
<th>Previous episodes of bowel obstruction</th>
<th>Diagnosis present obstruction</th>
<th>Criteria of inoperability</th>
<th>Doctors involved in the decision not to operate</th>
<th>Type of obstruction/level of obstruction</th>
<th>NGT removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 PC</td>
<td>None</td>
<td>Clinical + radiological</td>
<td>The patient refused surgery, poor PS, pleural effusion</td>
<td>PC doctors</td>
<td>Mechanical/large bowel</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical + previous surgery</td>
<td>Multiple sites of obstruction, previous laparotomy, ascites, peritoneal carcinomatosis</td>
<td>Surgeon + PC doctor</td>
<td>Mechanical + peritoneal carcinomatosis/small and large bowel</td>
<td>4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>9 AC</td>
<td>Exploratory laparotomy 12 days before T0</td>
<td>Clinical + radiological</td>
<td>Ascites, poor PS, previous laparotomy</td>
<td>Surgeon + PC doctor</td>
<td>Mechanical/small and large bowel</td>
<td>11&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>10 GF</td>
<td>Yes, resolved with NGT 15 days before T0</td>
<td>Clinical + radiological</td>
<td>Ascites, poor PS, multiple sites of obstruction</td>
<td>Surgeon + PC doctor</td>
<td>Mechanical/small and large bowel</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>11 CR</td>
<td>Yes, intestinal bypass with recanalization 10 days before T0</td>
<td>Clinical + radiological + previous surgery</td>
<td>Ascites, poor PS, previous laparotomy</td>
<td>Surgeon</td>
<td>Mechanical/small bowel</td>
<td>3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>12 FT</td>
<td>None</td>
<td>Clinical</td>
<td>Poor PS, ascites</td>
<td>Surgeon + PC doctor</td>
<td>Mechanical</td>
<td>4&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>13 PC</td>
<td>None</td>
<td>Clinical</td>
<td>Poor PS</td>
<td>PC doctor</td>
<td>Mechanical</td>
<td>13&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>14 AS</td>
<td>None</td>
<td>Clinical + radiological</td>
<td>Poor PS, ascites, cachexia, carcinomatosis</td>
<td>Surgeon</td>
<td>Mechanical + peritoneal carcinomatosis/small bowel</td>
<td>3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>15 FD</td>
<td>Yes, resolved with NGT 10 days before T0</td>
<td>Clinical + radiological</td>
<td>Poor PS, ascites, previous episodes of bowel obstruction, multiple obstructions, carcinomatosis</td>
<td>PC doctor</td>
<td>Mechanical + peritoneal carcinomatosis/small and large bowel</td>
<td>6&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>16 GD</td>
<td>Yes, resolved with NGT 12 days before T0</td>
<td>Clinical + radiological</td>
<td>Poor PS, peritoneal carcinomatosis</td>
<td>Surgeon + PC doctor</td>
<td>Peritoneal carcinomatosis</td>
<td>4&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>17 LC</td>
<td>Exploratory laparotomy</td>
<td>Clinical + radiological + previous surgery</td>
<td>Previous laparotomy, carcinomatosis</td>
<td>Surgeon</td>
<td>Peritoneal carcinomatosis/small bowel</td>
<td>7&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>PC = palliative care; PS = performance status.

<sup>b</sup>No. of day from T0.

<sup>c</sup>No. of days before death.
patients had already been undergoing analgesic treatment for some days before T0, and the dose of continuous subcutaneous morphine had to be increased at T1 in two patients without further change for the duration of the study.

Figure 2 shows the daily intensity of nausea, dry mouth, thirst, drowsiness, and feeling of abdominal distension in relation to the amount of parenteral hydration. This hydration was ≤500 ml for the Palermo patients and ≥2000 ml for the Milan patients; the figure depicts the four different assessment times.

Nausea intensity reported by the Palermo patients was significantly higher than the Milan patients at each time: T0, \( P = 0.002 \); T1, \( P = 0.001 \); T2, \( P = 0.003 \); and T3, \( P = 0.001 \). Nausea intensity in the 5 home care patients treated with OCT at T2 was lower (\( P = 0.05 \)) compared to that reported by the 5 home care patients on SB. There was no relation between the intensity of nausea and the OCT or SB treatment in the hospitalized patients.

There was no significant difference in dry mouth intensity in relation to the amount of parenteral hydration (Figure 2). No statistically significant difference in dry mouth was observed in the OCT patients and the SB patients; however, in SB patients, there was an upward trend in dry mouth.

Data regarding thirst intensity are available for all the Milan patients but only for 4 Palermo patients. There was a nonsignificant difference in the daily thirst intensity in relation to the amount of parenteral hydration at each time (Figure 2) and in relation to the treatment. However, there appeared to be an upward trend in thirst in the SB patients compared to the OCT patients, in whom there was a downward trend. We analyzed the 7 hospitalized patients, independently from the OCT or SB treatment, grouping them according to the amount of liquids consumed (equal to 250 ml/day [3 patients] vs. ≥600 ml/day [4 patients]). No significant difference was found in either group.

The home care patients showed an upward trend in drowsiness compared to the hospitalized, highly hydrated patients. The latter had significantly less intensity in drowsiness at T3 (\( P < 0.05 \)) (Figure 2). The intensity of drowsiness did not differ in OCT and SB groups.

The feeling of abdominal distension was not modified either by the amount of parenteral hydration (Figure 2) or by the OCT or SB
treatment. There was no significant variation in the intensity of dyspnea at each assessment time in all the patients under study, as well as in the patients divided according to treatment (OCT/SB) and to city group.

Discussion

The antisecretory and antiemetic efficacy of OCT has been described in patients with inoperable bowel obstruction.\textsuperscript{12–14,19} In some cases, this treatment allowed an NGT to be removed without further vomiting, even for patients with upper bowel obstructions, who are considered less responsive to medical treatment. SB has been shown to reduce GI secretions in patients with inoperable bowel obstruction,\textsuperscript{7,9,18} when the occlusion was not at the duodenal level.\textsuperscript{9} The results of our study confirm the capacity of both drugs to reduce GI secretions in patients with inoperable bowel obstruction,\textsuperscript{7,5,18} thus allowing the NGT to be removed in all home care patients and in the majority of the hospitalized patients, regardless of the level of the obstruction. For the home care patients, in whom it was possible to accurately compare the amount of the GI secretions, and thus the antisecretory activity of both drugs, OCT resulted in significantly reduced GI secretions by the second day of treatment. Although SB did not have a similar effect, the difference did not influence the number of days before NGT removal. Experimental studies suggest that the principal mechanism of fluid secretion in bowel obstruction depends on vasoactive intestinal peptide (VIP)-induced inflammatory events.\textsuperscript{29} OCT has been shown to have a potent anti-VIP effect resulting in the inhibition of intestinal secretion.\textsuperscript{30}

At the end of the study, it was only possible to remove the NGT in 3 of the 7 hospitalized patients without changing the dosage of the drugs. In 3 patients, it was possible to remove the NGT when the OCT dose was doubled (1 patient), when OCT was added to SB (1 patient), or when the SB dose was doubled and IV hydration was reduced (1 patient). Also, in these patients, OCT showed a trend toward better efficacy than SB.

Parenteral hydration use in the care of terminal cancer patients is still a controversial topic.\textsuperscript{31} In fact, the patients in Milan who were hospitalized received $\geq 2000$ ml of fluids intravenously daily compared to $\leq 500$ ml in the home care patients. These different approaches occurred despite the fact that all the patients were judged unfit for surgery, and had low performance status scores and a short life expectancy. The main goal of hydration is considered to meet the water/electrolyte baseline requirements and to correct or prevent symptoms related to dehydration, such as thirst, dry mouth, altered mental status (sometimes secondary to opioid metabolites), constipation, postural hypotension, and asthenia.\textsuperscript{32}

<table>
<thead>
<tr>
<th>Patients (No.)</th>
<th>Symptoms</th>
<th>T0 (mean)*</th>
<th>T1 (mean)*</th>
<th>T2 (mean)*</th>
<th>T3 (mean)*</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>Continuous pain\textsuperscript{a}</td>
<td>1.41</td>
<td>0.65</td>
<td>0.47</td>
<td>0.35</td>
<td>T0 vs. T1 P = 0.006</td>
</tr>
<tr>
<td>8 (treated with SB)</td>
<td>1.37</td>
<td>0.50</td>
<td>0.50</td>
<td>0.37</td>
<td>T0 vs. T2 P = 0.001</td>
<td></td>
</tr>
<tr>
<td>9 (treated with OCT)</td>
<td>1.44</td>
<td>0.78</td>
<td>0.44</td>
<td>0.33</td>
<td>T0 vs. T3 P = 0.039</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Colicky pain\textsuperscript{b}</td>
<td>0.76</td>
<td>0.29</td>
<td>0.25</td>
<td>0.12</td>
<td>T0 vs. T1 P = 0.005</td>
</tr>
<tr>
<td>8 (treated with SB)</td>
<td>0.87</td>
<td>0.37</td>
<td>0.28</td>
<td>0.14</td>
<td>T0 vs. T2 P = 0.011</td>
<td></td>
</tr>
<tr>
<td>9 (treated with OCT)</td>
<td>0.67</td>
<td>0.22</td>
<td>0.22</td>
<td>0.11</td>
<td>T0 vs. T3 P = 0.008</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Mean daily intensity of pain (4 test was not calculated).
\textsuperscript{b}P was evaluated between assessment times through the Mann-Whitney test.
\textsuperscript{c}No difference between treatment groups at T0, T1, T2, and T3 (P > 0.05).
\textsuperscript{d}No difference between treatment groups at T0, T1, T2, and T3 (P > 0.005).
Dry mouth is the subjective feeling of mouth dryness, and is not always accompanied by a detectable decrease in salivation. One of the causes of dry mouth is nasal blockage caused by an NGT and the reduction in mastication. Salivary flow is normal but the mouth feels dry to the patient because of fluid loss from rapid evaporation due to breathing through the mouth. Mastication plays an important role in the regulation of salivary secretion, with effects mediated through somatic afferent nerves of the oral mucosa and in the periodontal tissues. Patients taking a liquid diet or who have immobilized jaws following orthognatic surgery show a significant decrease in salivary flow. Moreover, SB can produce dry mouth because the muscarinic receptors are also present in human salivary glands. This can explain why patients on SB had a trend toward greater dry mouth intensity.

It is interesting to note that the hospitalized patients who received more IV and oral liquids reported the same intensity of thirst and dry mouth as those patients who received less IV hydration. In a prospective study, McCann et al. showed that fewer than 50% of terminally ill cancer patients experienced hunger or thirst due to inadequate food and water intake. In all patients, symptoms of hunger, thirst, and dry mouth could be alleviated through the provision of small amounts of food, fluids, and/or by the application of ice chips and lubrication to the lips. The quantity of liquid required was far less than that needed to prevent dehydration.

Our results agree with those of Burge, who showed that patients with advanced cancer receiving less fluid than 750 ml/day do not experience much more thirst than those receiving more than 750 ml/day. Contrary to the belief that thirst should increase with fluid deprivation, it has been shown that for every unit increase in fluid intake, there was a unit increase in the severity of thirst in cancer patients with advanced disease. Although the hospitalized patients received a large amount of IV fluids,
they also needed to drink much more liquid than the home care patients. It is possible that the higher quantity of IV and oral hydration taken by the hospitalized patients contributed to a more difficult removal of the NGT in these patients. This should be studied further.

Interestingly, the patients receiving large amounts of IV liquids had a significantly lower intensity of nausea at each assessment time and a nonsignificant downward trend in reduction of drowsiness, except for T3 when the reduction was statistically significant. Taking into consideration that the types and dosages of analgesics were overlapping and that, except for the amount of parenteral and oral hydration, there were no other differences in the pharmacological therapy between the two centers, it is possible that the nausea and drowsiness are due to accumulation of toxins produced in the GI tract in these patients with a nonworking bowel. Intravenous hydration could play an important role in reducing these symptoms.

It should be underlined that while the intensity of nausea was not different in the hospitalized patients on SB and on OCT, in the home care patients on OCT, the intensity of nausea was significantly lower at T2. In the hospitalized patients, the possible difference between the two antisecretory drugs may be overshadowed by the positive effect of IV hydration.

With respect to pain, it is interesting to note that during the period of the study, only 2 of the 17 patients required an increase of the dose of morphine at T1. SB and OCT reduce colicky pain through two different mechanisms, as previously described. Probably both drugs contribute indirectly to reducing the continuous abdominal pain through a decrease of GI secretions and, secondarily, abdominal distension.

Our study has limitations due to the small number of enrollable patients and the difficulty in correctly measuring the daily amount of NGT secretions in the hospitalized patients. Moreover, we designed the trial for a 3-day period only and did not include a crossover study because of the patients' poor conditions, which could worsen daily and create further problems in determining therapeutic efficacy. Furthermore, a crossover trial foresees a washout period between the two different treatments and this is not recommended in patients with advanced cancer.

We conclude that all the patients with inoperable malignant bowel obstruction should undergo antisecretory drug treatment to evaluate the possibility of avoiding or removing the NGT. The OCT should be considered as the first-choice antisecretory drug when a rapid reduction in GI secretions is necessary. However, the cost of the two drugs must be considered. In many countries, the cost of 0.3 mg OCT is $37.73US, whereas the cost of 60 mg SB is $1.35US. The cost of a drug should be interpreted in the widest possible sense. That is, if the use of a drug results in a more rapid improvement of GI symptoms, which potentially reduces hospital stay or the admission to an inpatient unit, or leads to a better quality of life, these factors should be considered when calculating cost.

Further well-designed studies are necessary to better evaluate the role of IV hydration, not only in symptom control but also regarding a possible influence in increasing GI secretions in patients with malignant inoperable bowel obstruction. Moreover, it would be interesting to evaluate the antisecretory effects and the time required to remove the NGT on administering OCT and SB from the beginning of the treatment of bowel-obstructed patients.

Acknowledgment

This study was supported, in part, by the Italian Association for Cancer Research, Grant N. AIRC 198512.

References


4. van Ooijen B, van der Burg MEL, Planting ASTh, Siersema PD, Wiggers T. Surgical treatment or gastric drainage only for intestinal obstruction in patients with carcinoma of the ovary or peritoneal car-


