RESEARCH ARTICLE

Clinical Impact of Palliative Treatment Using Octreotide for Inoperable Malignant Bowel Obstruction Caused by Advanced Urological Cancer

Hiroki Kubota[1]*, Kazumi Taguchi[2], Daichi Kobayashi[2], Hiromichi Naruyama[1], Masahito Hirose[1], Katsuhiro Fukuta[1], Yasue Kubota[2], Takahiro Yasui[2], Yasuyuki Yamada[1], Kenjiro Kohri[2]

Abstract

Malignant bowel obstruction (MBO), an occasional complication in patients with advanced urological cancer, causes gastrointestinal symptoms such as nausea and vomiting leading to suffering which severely impairs quality of life (QOL) . Drug therapy, especially octreotide, a synthetic analog of somatostatin, is reportedly effective in controlling the symptoms of MBO. In the present study, we administered octreotide to urological cancer patients with MBO and evaluated the improvement of subjective symptoms, oral intake, and nasogastric intubation. Fourteen terminally ill urological cancer patients suffering with MBO were included (age range 55-92, 10 male, 4 female). Octreotide was administered at 300μg/day to those patients subcutaneously as a continuous injection. Significant improvements in subjective symptoms were observed in thirteen patients (92.8%), and ten patients (71.4%) were able to resume oral intake. Four patients required nasogastric drainage before the administration of octreotide, but nasogastric intubation was discontinued in all these cases after the use of octreotide. Early initiation of octreotide resulted in better improvement of MBO symptoms, and no adverse event was observed in any of the patients. These results revealed that 300μg/day dose of octreotide is safe and effective for managing gastrointestinal symptoms of terminally ill urological cancer patients with MBO. We also recommend starting the treatment with ocreotide as soon as MBO is diagnosed.

Keywords: Malignant bowel obstruction - octreotide - quality of life - urological cancer - palliative care

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Introduction

With an increase in the number of patients with malignant tumors, managing various symptoms of terminal ill cancer patients has become essential. Malignant bowel obstruction (MBO) is a serious complication commonly observed in advanced gastrointestinal or ovarian cancer patients. MBO interferes with the oral intake of food and causes painful symptoms such as nausea, vomiting, and abdominal pain. Therefore, patients' quality of life (QOL) is significantly impaired. Palliation of symptoms from obstruction has traditionally been performed by gastrointestinal drainage and total parenteral nutrition. Surgical management has also been considered in patients with significant life expectancy (Davis and Nouneh, 2000; Ripamonti and Mercadante, 2005; Tuca et al., 2012).

Current treatments for inoperable patients with MBO include medication in addition to gastric or intestinal intubation. However, drug therapy such as antiemetics has not achieved satisfactory effects in palliating the symptoms of MBO. The somatostatin analogue, octreotide (Sandostatin®, Novartis Pharmaceuticals Corporation, Switzerland), has been reported to suppress secretion of gastrointestinal hormones and improve gastrointestinal motility, and exhibit proabsorptive effect on the intestinal mucosa. The efficacy of octreotide in controlling the symptoms of MBO has been shown in several reports (Davis and Nouneh, 2000; Ripamonti and Mercadante, 2005; Mercadante et al., 2007; O'Connor and Creedon, 2011; Mercadante and Porzio, 2012).

Although the frequency of MBO in urological cancer is unknown, MBO is not rare statement for terminally ill urological cancer patients. We urologists should pay attention to managing MBO symptoms and shoulder the important responsibility of maintaining quality of life (QOL) in these patients. In this study, we investigated the effectiveness of octreotide in urological cancer patients with MBO and evaluated the changes in subjective symptoms such as nausea and vomiting, oral intake of food, and nasogastric intubation.

*[1]Department of Urology, Kainan Hospital, Yatomi, [2]Department of Nephro-urology, Nagoya City University Graduate School of Medical Science, Nagoya, Japan *For correspondence: urokubo@gmail.com*

Materials and Methods

This study included fourteen patients admitted to our hospital between July 2008 and June 2011 with MBO due to advanced urological cancer. The diagnosis of bowel obstruction was initially made on the basis of clinical symptoms of nausea, vomiting, abdominal pain, signs of abdominal distension and obstructive bowel sounds. Then radiological evidence of bowel obstruction was also obtained from all patients. Abdominal X-ray films and computed tomography scans showed that the distension of intestinal lumens and the typical images of water-air levels. Of the fourteen patients, ten were males and four were females. The mean age was 79.4 years (range: 55-92 years). Urothelial carcinoma and locally invasive prostate cancer were the primary diseases in most cases. All patients were terminally ill and palliative surgery was performed in only one case, but without achieving total relief of symptoms. Four patients were treated with nasogastric drainage. Further details of the patients are summarized in Table 1.

Octreotide was subcutaneously administered at a dose of 300 μg/day as a continuous infusion. We did not administer corticosteroid concurrently with octreotide to the patients. According to department policy, the patients were hydrated with 1000 mL of saline and glucose solutions intravenously. No patients received a parenteral nutrition. Nasogastric tubes were removed if the daily drainage volume decreased to less than 100 mL/day. Subjective symptoms were assessed using the World Health Organization toxicity grading system (Table 2) (WHO, 1979). When the WHO grade was reduced to 0, the response was regarded as "complete response", and improvement of more than one grade was regarded as "partial response". Improvement of less than two grades was regarded as "no change". The quantity and content of the intake were also investigated if the patients resumed oral intake.

Results

The treatment results are presented in Table 3. The mean duration of octreotide administration was 16 days (range: 4-47 days). The control of vomiting was generally rapid, and the mean time to produce an effect was 1.6 days (range: 1-5 days). Improvement in subjective symptoms according to the WHO grading was regarded as "partial response" in nine patients (64.3%) and "complete response" in four patients (28.6%). One patient was regarded as "no change" because his symptom improved only one grade. He was in poor general condition, and died six days after hospitalization. Overall response rate (complete response + partial response) was 92.8% (95% confidence interval: 76-100%).

No significant relevance was recognized between the response rate and the primary site of tumor or the major site of obstruction. The period from the diagnosis of MBO to the initiation of octreotide treatment in patients with "complete response" was significantly shorter than that in patients with "partial response" (5.0 days vs. 9.2 days,

Table 2. Grading of Vomiting by the World Health Organization Toxicity Criteria

Grade	Nausea Vomiting
0	no nausea and vomiting
1	nausea
2	transient vomiting
3	vomiting requiring therapy
4	intractable vomiting

Table 3. Response

Patient No	Pretreatment emesis (day)	Duration of octreotide treatment (day)	Time to produce an effect (day)	WHO grading after treatment	Response	Resuming oral intake (Y/N)	Contents of oral intake
1	7	38	1	0	CR	Y	Regular diet
2	3	38	5	0	CR	Y	Soft diet
3	14	9	2	1	PR	Y	Liquid diet
4	4	18	1	2	PR	Y	Regular diet
5	9	4	1	2	PR	Y	Liquid diet
6	21	6	3	2	NC	Y	Soft diet
7	7	4	1	1	PR	N	
8	5	5	1	1	PR	Y	Liquid diet
9	6	18	1	0	CR	Y	Liquid diet
10	4	7	1	0	CR	Y	Soft diet
11	10	10	2	1	PR	N	
12	11	47	1	2	PR	Y	Liquid diet
13	6	7	2	1	PR	N	
14	5	13	1	1	PR	N	

Table 1. Demographic and Baseline Characteristics of the Patients

Patient No.	Age	Sex	Primary site of tumor	Major site of obstruction	Surgical treatment of MBO (Y/N)	Nasogastric tube at baseline (Y/N)	Performance status	WHO grading at baseline
1	85	F	Bladder	Small intestine	Y	N	2	3
2	80	F	Ureter	Colon	N	N	3	2
3	76	M	Bladder	Small intestine	N	Y	2	3
4	81	M	Bladder	Small intestine	N	Y	2	4
5	83	M	Bladder	Colon	N	N	3	4
6	92	M	Prostate	Colon	N	N	4	3
7	84	M	Bladder	Small intestine	N	Y	3	3
8	55	M	Prostate	Colon	N	N	2	3
9	80	M	Prostate	Colon	N	N	2	2
10	86	F	Bladder	Small intestine	N	N	3	2
11	85	F	Bladder	Small intestine	N	Y	3	3
12	81	M	Bladder	Small intestine	N	N	3	4
13	65	M	Kidney	Small intestine	N	N	3	3
14	78	M	Bladder	Undetermined	N	N	2	3

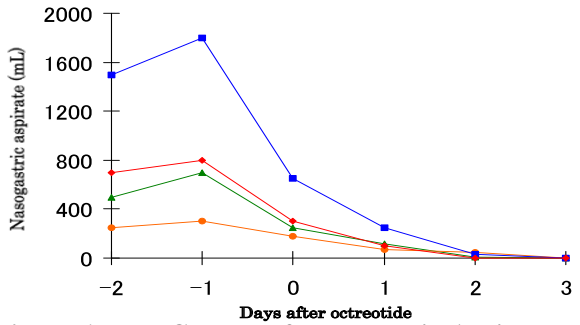

Figure 1. The Change of Nasogastric Aspirates of Patients Being Treated with Nasogastric Drainage

p=0.036). Ten of fourteen patients (71.4%) were able to resume oral intake of food. Two patients (No.1 and No.4) could take regular diet, and discharged from hospital for 35 days and 74 days, respectively.

Figure 1 demonstrates the reduction of nasogastric aspirate in patients who had nasogastric drainage. Nasogastric tubes were finally removed in all four patients within three days after the administration of octreotide. Three of four patients resumed oral intake including small amount of liquid diet.

No adverse event related to octreotide treatment was observed in all patients. Almost all patients finally died with minimal distress or pain.

Discussion

MBO is a common complication in patients with terminal digestive organ and gynecological cancers. MBO frequencies ranging from 20% to 50% in ovarian cancer and from 10% to 29% in colorectal cancer have been reported (Tuca et al, 2012). MBO has been reported to occur because of obstruction caused by tumor, edema, and fibrosis induced by cancerous peritonitis. Complications of a dilated bowel include supersecretion of digestive fluids and decreased absorptive capacity of the gastrointestinal tract. Symptoms such as nausea, vomiting, abdominal fullness, and pain are common. MBO frequencies in urological cancers have not been determined, but the condition may be fairly widespread.

Octreotide is a somatostatin analog derived from intestinal epithelial cells and is known to suppress the secretion of growth and gastrointestinal hormones (Ripamonti and Mercadantes, 2005; Mercadante and Porzio, 2012). Octreotide also suppresses the secretion of digestive fluids and promotes water and electrolyte absorption. These effects of octreotide lead to alleviation of MBO symptoms by limiting the vicious cycle of distention and secretion (Khoo et al., 1994; Ripamonti and Mercadante, 2005; Mercadante et al., 2007; Mercadante and Porzio, 2012). The efficacy of octreotide in MBO management has been frequently reported in gastrointestinal and ovarian cancers, but not in urological cancer (Ripamonti et al., 2000; Mystakidou et al., 2002; Mercadante et al., 2004).

In the present study, we evaluated the effects of octreotide on MBO in urological cancer. Rapid relief of symptoms was achieved in most patients within 1-5 days, more commonly within 2 days. Overall response rate was satisfactory compared with previous reports (Khoo et al., 1994; Ripamonti et al., 2000; Mystakidou et al., 2002; Hisanaga et al, 2010). The results indicated that octreotide was effective in managing MBO symptoms in urological cancer. Our data also suggests that early administration of octreotide was more effective in managing MBO symptoms. All the patients with complete response received octreotide treatment within seven days after they complained of nausea and vomiting. Although MBO is reversible in many cases, it can become irreversible because of accumulation of feces and formation of edema (Mercadantes et al., 2004). Especially in patients with poor general status, the efficacy of medical therapy and fluid administration is often limited. Therefore, the treatment of MBO should commence as early as possible.

Corticosteroids reduce inflammation and edema of the gastrointestinal tract associated with MBO. Certain reports suggest that administration of dexamethasone alone is effective in controlling MBO symptoms (Mercadante et al., 2004; Tuca et al, 2012). However, the effects of octreotide and corticosteroids on MBO have not been compared. Further research is needed to examine the role of corticosteroids in MBO treatment (Mercadante et al., 2007; O'Connor and Creedon, 2011). Combination therapy of octreotide and corticosteroids has been studied empirically, but there is not enough data to support its efficacy. Thus, corticosteroid was not administered concurrently with octreotide in the present study.

Appropriate administration of intravenous fluids is indicated to improve nausea and vomiting if the patient's overall status is good (Mercadante et al., 2000; Bozzetti et al., 2002). However, vomiting can increase due to excess infusion volume (Philip and Depczynski, 1997). Therefore, the use of hydration remains controversial and should be decided on individual basis (O'Connor and Creedon, 2011). Combined use of intravenous fluids and octreotide is recommended because the efficacy of intravenous fluids alone is limited.

Octreotide has few side effects and is easy to administer. Urologists who are inexperienced in managing digestive symptoms find it usable. Based on the obtained results, we believe that octreotide is effective in managing symptoms of terminally ill urological cancer patients with MBO. Therefore, we recommend the early use of octreotide in MBO to improve QOL of terminally ill urological cancer patients.

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