

BCCA Guidelines for Management of Chemotherapy-induced Diarrhea

Introduction

Patients receiving chemotherapy or radiation are at high risk for developing diarrhea, which is estimated to be as high as 45% with chemotherapeutic drugs like irinotecan or 5-fluorouracil (5FU). This side effect often leads to delay in treatment, dose reduction or discontinuation of treatment. There is a small but significant mortality associated with chemotherapy-induced diarrhea (CID), especially when it occurs concomitantly with mucositis and neutropenia.

Classification

CID is graded using the NCI criteria (Table 1) which grades diarrhea on a scale of 0 (normal) to 4 (severe) according to the number of loose stools/days, presence of nocturnal stools, incontinence, cramping and blood in stools.

Table 1 NCI criteria for assessment of chemotherapy-induced diarrhea

Grade	0	1	2	3	4
No. of stools/day	Normal	2 – 3	4 - 6	7 - 9	>10
Symptom	-	-	Nocturnal stools	Incontinence	Bloody stool
	-	-	Moderate cramping	Severe cramping	Need for parenteral fluid support

Risk factors

Certain factors appear to be associated with an increased incidence of CID.

Patient factors

- Older age
- Female gender
- Lower performance status (ECOG 2 or more)
- Associated bowel pathology (e.g colitis, lactose intolerance)
- Presence of tumor in bowel

Therapy-related factors

- Drugs: irinotecan and 5FU
- Weekly chemotherapy schedule
- Infusional chemotherapy
- Prior history of CID
- Concomitant abdominal-pelvic radiation and chemotherapy

Management

CID can be a serious complication and requires prompt assessment. The steps in this assessment are as follows:

1. Rule out other or concomitant causes of diarrhea

Other causes of diarrhea must be ruled out. These include medications (e.g. stool softeners, laxatives, antacids, etc), infection by *C. difficile* or *Candida* species, partial bowel obstruction, malabsorption, fecal impaction, acute radiation reaction and surgery (short bowel syndrome). Diets high in fiber or lactose may aggravate diarrhea.

2. Dietary modifications during diarrhea

Mild diarrhea may be managed with diet to decrease the frequency of stools. Patients should be advised to increase intake of clear fluids (e.g. water, sports drinks, broth, gelatin, clear juices, decaffeinated tea, caffeine-free soft drinks). A BRAT (banana, rice, apples, toast) diet can be helpful.

(Note that patients who develop diarrhea while on irinotecan chemotherapy should be treated promptly with high-dose loperamide as outlined below, and dietary management alone is inadequate.)

3. Medications

a. Loperamide

Loperamide is indicated for Grade 1 diarrhea that persists for more than 12-24 hours or for moderate diarrhea (Grade 2). The standard dose of loperamide is 4 mg followed by 2 mg every 4 hours or after each unformed stool (maximum dose 16 mg/day). This dose may be increased in patients with mild to moderate diarrhea (Grade 1 or 2) that persists for more than 24 hours. The dose is 4 mg to start, followed by 2 mg every 2 hours (or 4 mg every 4 hours at night to allow sleep). Loperamide should be continued for 12 hours following resolution of the diarrhea and re-establishment of a normal diet.

High-dose loperamide (4 mg followed by 2 mg every 2 hours) is also recommended at the onset of *any* diarrhea in patients receiving irinotecan chemotherapy.

b. Atropine-diphenoxylate (Lomotil®)

At the discretion of the treating physician, it may be useful to add atropine-diphenoxylate 1 to 2 tablets, every 6-8 hours, to loperamide therapy for Grade 1 or 2 diarrhea. It should not be expected that this would be sufficient for the management of Grade 3 or 4 diarrhea.

c. Octreotide

For Grades 1 and 2 diarrhea lasting more than 24 hours despite high-dose loperamide \pm atropine-diphenoxylate, octreotide 100-150 mcg SC TID may be considered (Table 2). For Grades 3 and 4 diarrhea, octreotide 150 mcg SC TID is indicated; these patients usually require hospitalization (Table 3). If there is no improvement in the diarrhea after 24 hours, the dose of octreotide should be increased to 300-500 mcg SC TID. The

duration of octreotide therapy should be individualized, but can be discontinued 24 hours after the end of diarrhea and re-establishment of a normal diet.

d. Antibiotics

In the presence of concomitant neutropenia (granulocytes $<1 \times 10^6/L$), antibiotics (e.g. ciprofloxacin 500 mg BID) should be considered until resolution of diarrhea and recovery of the granulocyte counts.

Table 2 Management of Grades 1 and 2 chemotherapy-induced diarrhea

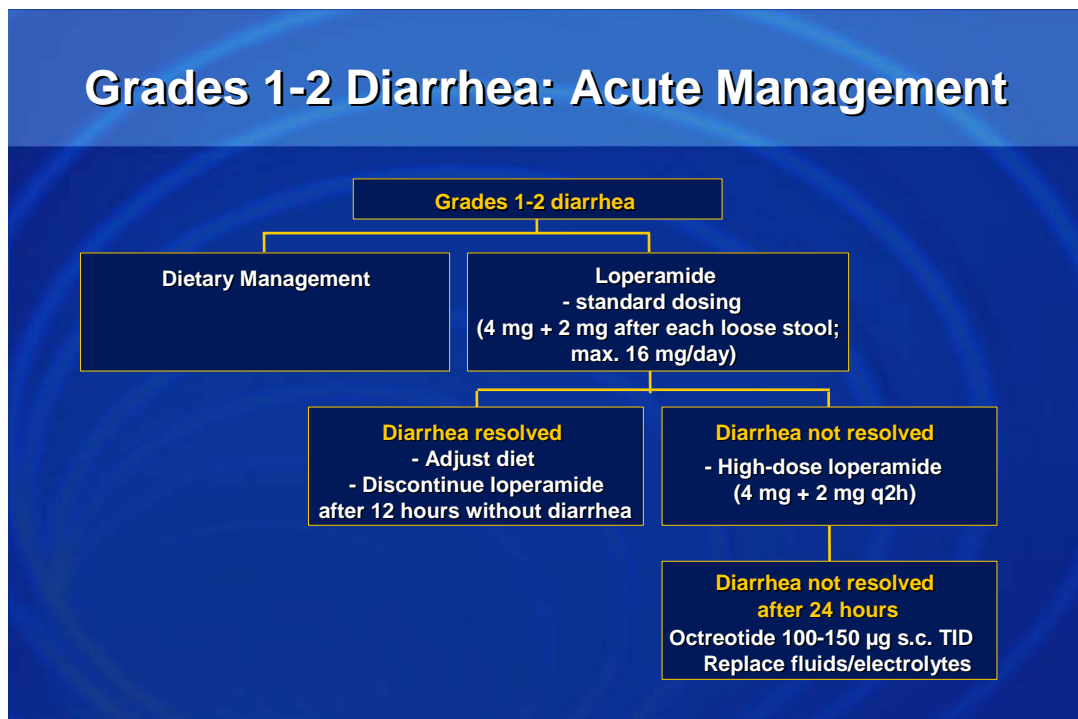
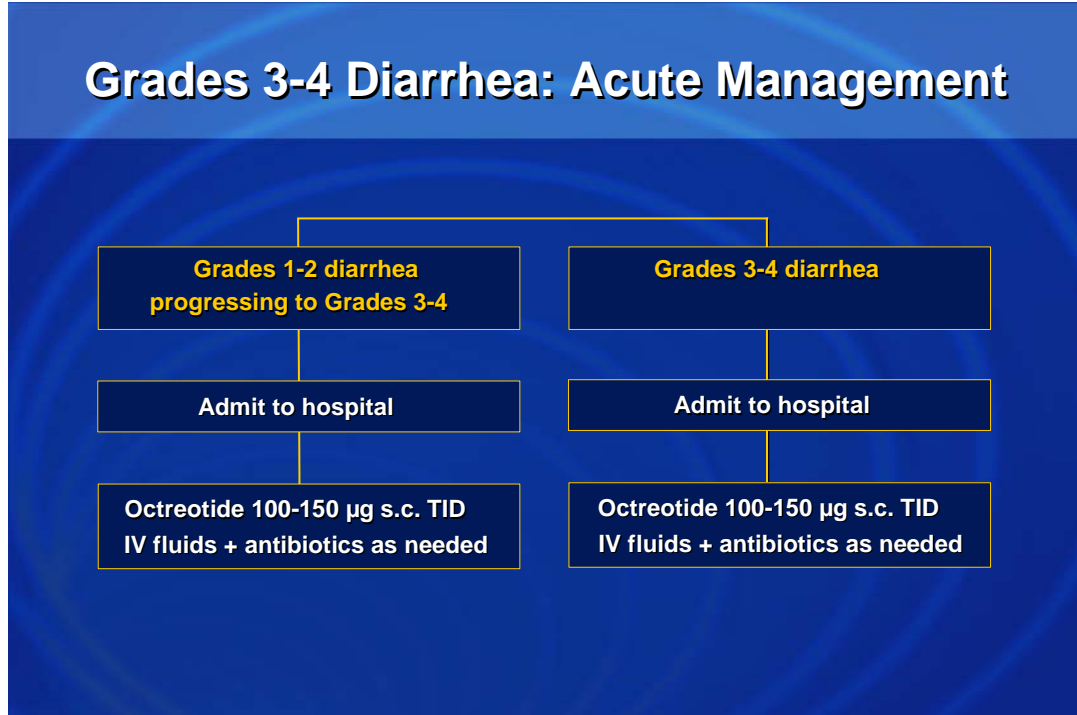


Table 3 Management of grade 3-4 chemotherapy-induced diarrhea



Call Dr. Amil Shah @ (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: **14 October 2004**

Date revised:

References

- Arbuckle RB, Huber SL, Zacker C. The consequences of diarrhea occurring during chemotherapy for colorectal cancer: a retrospective study. *Oncologist* 2000;5:250-9.
- Benson AB, Ajani JA, Catalano RB. Recommended guidelines for treatment of cancer treatment-induced diarrhea. *J Clin Oncol* 2004; 22: 2918-26.
- Cascinu S, Barni S, Labianca R. Evaluation of factors influencing 5-Fluorouracil-induced diarrhea in colorectal cancer patients. An Italian Group for the Study of Digestive Tract Cancer study. *Support Care Cancer* 1997;5:314-7.
- Rothenberg ML, Meropol NJ, Poplin EA. Mortality associated with irinotecan plus bolus fluorouracil/leucovorin: Summary findings of an independent panel. *J Clin Oncol* 2110;19:3801-7.
- Rosenoff S. Octreotide LAR resolves severe chemotherapy-induced diarrhea and allows continuation of full-dose therapy. *Proc Am Soc Oncol* 2003;22:778 (abstr 3126).
- Wadler S, Benson AB, Engelking C. Recommended guidelines for the treatment of chemotherapy-induced diarrhea. *J Clin Oncol* 1998;16:3169-78.