Clinical Snapshot: Diarrhea

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Management of Chemotherapy-Induced Diarrhea

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Chemotherapy-induced diarrhea (CID) is a complication of several chemotherapeutic agents, most notably the fluoropyrimidines (Buroker, O'Connell, Wieand, et al., 1994) and topoisomerase I inhibitors (Saltz, Cox, Blanke, et al., 2000). Early intervention is the key to optimal management and prevention of dehydration, electrolyte imbalances, and associated sequelae. Without proper management, CID can have a negative impact on patient quality of life and treatment outcomes.

Pathophysiology

The etiology of CID is not clearly understood. It is thought that chemotherapy toxicity initiates the destruction or alteration of rapidly dividing crypt cells in the intestinal epithelium, thereby inhibiting its absorptive capacity and leading to diarrhea. The disruption between the balance of absorptive and secretory abilities can result in increased loss of fluid and electrolytes through the stool (Saltz, 2003).

Definition and Assessment

Although there are different definitions of diarrhea, the mainstay is from the Common Terminology Criteria for Adverse Events (CTCAE), which states that diarrhea is a disorder characterized by frequent and watery bowel movements (National Cancer Institute, 2009). The CTCAE bases this definition on the amount of stools above what is normal for the patient. A grading system of 1 through 5 is utilized to identify severity of diarrhea, with 1 being mild and 5 equivalent to death, as shown in Table 1.

Table 1

Common Terminology Criteria for Adverse Events Reporting: Diarrhea (Version 4.2)

Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Diarrhea	Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4–6 stools per day over baseline; moderate ostomy output compared to baseline	Increase of ≥ 7 stools per day; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADLs	Life-threatening consequences; urgent intervention needed	Death

Note. ADLs = activities of daily living. A semicolon indicates "or" in the grade description. Based on information from the National Cancer Institute, 2009.

A thorough evaluation of diarrhea begins with a comprehensive history, exploration of patient-reported symptoms, dehydration assessment, and physical exam. Assessment strategies are outlined in Table 2.

Table 2

Assessment Tools for Diarrhea

Comprehesive History	Patient Report	Dehydration Evaluation	Physical Exam
Cancer diagnosis and past/current treatment Review of complete medication list including medications stopped within the past month: laxatives, opioids, antibiotics, regular and as-needed medications, herbal and over-the-counter medications, vitamins and supplements, chemotherapy and biotherapy agents	Description of baseline and current bowel movements Probe for specifics including when change in patterns began; frequency, amount, consistency, and color of stool; incontinence episodes; presence of blood in stool and distinct odor associated with stool	Objective assessment: assess orthostatic hypertension, weight loss, skin turgor, dry mucous membranes Subjective assessment: dizziness, weakness, excessive thirst, decreased urination	Palpate abdomen for tenderness Percuss: dullness may indicate obstruction or fecal impaction Auscultate for bowel sounds

Note. Adapted from Grande, 2009.

Management

Management of diarrhea is integral from first onset and includes both pharmacologic and nonpharmacologic interventions. A variety of antidiarrheal agents are available for intervention of CID. These agents are classified on the basis of mechanism of action. These categories include opioids such as diphenoxylate and atropine (e.g., Lomotil), codeine, opium tincture, and paregoric. Nonopiods include loperamide (e.g., Imodium). The absorbents include bismuth subsalicylate (e.g., kaopectate). The last category includes the somatostatin analog octreotide.

In 1998, expert oncology clinicians who participated in a closed roundtable meeting developed and published comprehensive guidelines for CID assessment and management (Wadler, Benson, Engelking, et al., 1998). This group reconvened in 2002 to broaden the scope of the evidence-based guidelines by incorporating radiation-induced diarrhea and updating with data published since the original guidelines (Benson, Ajani, Catalano, et al., 2004). Highlights of treatment for CID are included in Table 3.

Table 3

Management of Chemotherapy-Induced Diarrhea

Assessment	Pharmacologic Intervention	Nonpharmacologic Intervention
Grade 1-2 diarrhea	Loperamide: initial dose 4 mg followed by 2 mg every 4 hours or after every unformed stool	Stop all caffeine or lactose-containing products, alcohol, and high osmolar supplements Drink 64–100 oz of liquids a day (Gatorade or broth) Eat frequent, small meals of bananas, rice, applesauce, toast (BRAT diet) or plain pasta If grade 2: hold cytotoxic chemotherapy until symptoms resolve, and consider dose reduction
Assess 12–24 hours later: Diarrhea improving	Discontinue loperamide after 12-hour diarrhea-free interval	Continue dietary modification Gradually add solid foods to diet
Assess 12–24 hours later: Diarrhea not improving	Diarrhea remains grades 1-2: Continue loperamide 2 mg every 2 hours Start oral antibiotics Diarrhea progresses to grades 3-4: Admit to the hospital Initiate octreotide 100–150 mcg subcutaneously three times a day or intravenously 25–50 mg/hr Start IV fluids and antibiotics as needed Evaluate stool, CBC, and electrolyte levels Discontinue cytotoxic chemotherapy until all symptoms resolve, restart at reduced dose	Diarrhea remains grades 1-2: Continue with current dietary restrictions

Note. CBC = complete blood count. Adapted from Benson, Ajani, Catalano, et al., 2004.

Role of the Advanced Oncology Practitioner

The role of the advanced oncology practitioner is crucial in educating patients regarding the potential side effects their chemotherapy treatments may trigger. Early assessment and appropriate intervention are crucial steps in averting life-threatening or irreversible consequences.

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