Symptom Management Guidelines: DIARRHEA

NCI CTCAE GRADE AND MANAGEMENT | RESOURCES | CONTRIBUTING FACTORS | APPENDIX

Definition

Cancer – Related Diarrhea (CRD): An abnormal increase in stool frequency, volume, and liquidity that is different from the usual patterns of bowel elimination; results from cancer or related treatment(s).

FOCUSED HEALTH ASSESSMENT

PHYSICAL ASSESSMENT

Vital Signs
- As clinically indicated

Weight
- Take current weight and compare to pre – treatment or last recorded weight
- Calculate Body Mass Index (BMI)

Hydration Status
- Skin turgor, capillary refill, mucous membranes
- Assess for:
  - amount and character of urine
  - daily intake and output
  - thirst and dry mouth
  - weakness and dizziness
  - most recent lab results

Abdominal Assessment
- Auscultate abdomen - assess presence and quality of bowel sounds
- Abdominal pain, tenderness, distention

Stool Examination
- Inspect stool for colour (visible blood or mucous), consistency, volume, and odour

Skin Integrity
- Perineal or peristomal skin integrity
- Note any areas of erythema, edema, exudates, bleeding or skin breakdown

Mental Status
- Confusion, alterations in level of consciousness

Functional Status
- Activity level/ECOG or PPS

SYMPTOM ASSESSMENT

Normal
- What are your normal bowel habits?
- Do you have an ostomy? If so, how many times do you normally empty/change the bag?
- Are you aware of any medications that you are taking that could cause diarrhea?

Onset
- When did diarrhea begin?
- How many bowel movements in the last 24 hours?
- If ostomy, how many times did you empty/change bag?

Provoking / Palliating
- What brings on the diarrhea?
- Anything that makes the diarrhea better? Worse?

Quality
- Describe your last bowel movement
  - Was there any blood or mucous?
  - Was it loose or watery?
  - Can you estimate the amount, large or small volume?
  - Can you describe the odour?

Region / Radiation- N/A

Severity / Other Symptoms
- How bothered are you by this symptom? (on a scale of 0 – 10, with 0 being not at all to 10 being the worst)
- Have you been experiencing any:
  - Abdominal cramping
  - Diarrhea overnight (nocturnal stools)
  - Incontinence of stool
  - Fever - possible infection
  - Dry mouth, thirst, dizziness, weakness, dark urine -possible dehydration
  - Severe abdominal pain, bloating, nausea, vomiting - possible bowel obstruction
  - Skin breakdown around your rectum/colostomy
- Are you able to keep fluids down? What are you drinking? How much? What is your dietary intake? Are you urinating normally?

Treatment
- What medications or treatments have you tried? Has this been effective?

Understanding / Impact on You
- Is your diarrhea interfering with your normal daily activity (ADLs)?

Value - What do you believe is causing your diarrhea?

DIARRHEA GRADING SCALE NCI Common Terminology Criteria for Adverse Events (CTCAE) (Version 5.0)				
GRADE 1 (Mild)	**GRADE 2 (Moderate)**	**GRADE 3 (Severe)**	**GRADE 4 (Life - threatening)**	**GRADE 5**
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 increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of >=7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL	Life threatening consequences; urgent intervention indicated	Death

Special Considerations for Irinotecan	
Early Onset Diarrhea	• Occurs during or within 24h of administration • Cholinergic response that may be accompanied with other symptoms such as abdominal cramping, diaphoresis watery eyes, salivation, and rhinitis. Manage symptoms with Atropine. • Instruct patient to contact healthcare providers (BC Cancer Nurse Telephone Line or Physician on call) to determine whether patient needs to come to cancer agency or go to emergency department for atropine treatment • Prophylactic atropine may be indicated for subsequent treatments
Late Onset/Delayed Diarrhea	• Occurs more than 24h after administration • Can be prolonged and lead to potentially life–threatening dehydration and electrolyte imbalance if not proactively managed • Must be treated immediately with high dose loperamide • Patient Education: - Always keep supply of loperamide at home (available at pharmacy without a prescription) - Take two tablets (4 mg) after 1st loose stool then one tablet (2 mg) every 2h until diarrhea-free for 12h - Overnight may take 4 mg every 4h to allow longer sleep period - Loperamide daily dosage may exceed package recommendations. Reinforce importance of taking higher dosage to stop diarrhea - Contact healthcare providers (BC Cancer Nurse Telephone Line or Physician) if diarrhea does not improve within 24h after starting loperamide or if diarrhea lasts more than 36h (as antibiotics may be prescribed)
Special Considerations for Immunotherapy (Checkpoint Inhibitors)	
Immune-Mediated Adverse Reactions	• Can cause **severe and fatal** immune-mediated adverse reactions including: enterocolitis, intestinal perforation, hepatitis, dermatitis, neuropathy, endocrinopathy, and toxicities in other organ systems • Permanent discontinuation of treatment is recommended for severe immune-mediated reactions • Onset usually occurs during the beginning of treatment, but may occur months after last dose • All patients should be given an immunotherapy alert card, Immunotherapy Patient Letter, and SCIMMUNE patient handout when treatment is started
Special Considerations for Immunotherapy (Bispecific Antibodies)	
Overactivation and dysregulation of immune system	• Diarrhea may be a sign and symptom of cytokine release syndrome • Prompt recognition and intervention are critical to prevent progression of symptoms • Refer to SCCRS protocol for directions on symptomatic treatment • All patients should be given bispecific antibodies alert card, bispecific antibodies patient letter, and SCCRS/SCICANS patient handout when treatment is started

***Step-Up Approach to Symptom Management:**
Interventions Should Be Based On Current Grade Level and Include Lower Level Grade Interventions As Appropriate

NORMAL
GRADE 1
(First 24 hours of onset)

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NON – URGENT:

Prevention, support, teaching, & follow-up as clinically indicated

Patient Care and Assessment	• Assess pattern (number of days diarrhea present), characteristic of stool (amount, color, consistency) • If patients are on checkpoint inhibitors, diarrhea may not be a direct side effect of the treatment, but rather a product of immune mediated side effects. • If patients are on bispecific antibodies, diarrhea may not be a direct side effect of the treatment, but rather a symptom related to CRS. • Assessment and management of contributing factors, if irinotecan, checkpoint inhibitor, or bispecific antibody-related ***See special considerations for patients on Irinotecan, Checkpoint Inhibitor, or Bispecific antibodies*** • Collaborate with physician to rule out other causes or concomitant causes of diarrhea and to determine if further investigation warranted
Dietary and Lifestyle Management	**Encourage:** - 10-12 cups of clear fluids throughout the day (water, sports drinks, diluted juice, broth) - Soluble fiber (e.g. peeled apples and pears, bananas, potatoes, applesauce, white rice and pasta, oatmeal) - Small, frequent meals **Reduce:** - Insoluble fibre (skins of fruits and vegetables, leafy greens, nuts and seeds) - Caffeine (tea, coffee, pop, energy drinks) - High sugar beverages (juice, iced tea, pop) - Gas-forming foods (broccoli, carbonated beverages) - High fat dairy **Avoid:** - Spicy foods - Deep fried, greasy foods - Sorbitol-containing substances (e.g. sugar-free gums and candy) - Alcohol
Pharmacological Management	• Avoid/discontinue any medications that may cause or exacerbate diarrhea (e.g. bulk laxatives, metoclopramide) in collaboration with physician and pharmacist • If patient is taking warfarin, in collaboration with physician, consider increasing frequency of INR monitoring • Instruct patient to start or continue loperamide according to package directions or as indicated by physician: - Start with 4 mg, followed by 2 mg every 4h or after each unformed stool (Max daily dose: 16 mg, unless directed otherwise by physician) - Continue loperamide until 12h diarrhea-free (or as otherwise advised by physician) - Patients with RT-induced diarrhea may continue loperamide for duration of treatment

	* Corticosteroids (Refer to protocol specific algorithm if patient is on checkpoint inhibitor) *<u>***See special considerations for patients on Irinotecan, Checkpoint Inhibitor, or Bispecific antibodies***</u>
Skin Care Management	• Protect skin integrity and promote self-care • Cleanse perianal skin with warm water (+/- mild soap) after each stool, pat dry, do not rub • Encourage sitz bath as tolerated with tepid water • Moisture barrier creams prn
Patient Education	• Record onset and number of loose stools per 24hr • Reinforce: – Diarrhea can be effectively managed with prompt intervention – Importance of accurately reporting diarrhea – To seek immediate medical attention if: ➢ T ≥ 38° C / 100º F ➢ Bloody stools ➢ Severe cramping, acute abdominal pain (+/- nausea and vomiting) ➢ Dizziness, weakness, confusion, excessive thirst, dark urine ➢ Diarrhea or increased ostomy output not improving with recommended strategies • Inform patient that isolation precautions may be required if symptoms worsen or infection suspected, patient may need to be isolated as per Infection Prevention and Control guidelines • Encourage patients to perform proper hand hygiene to prevent the spread of micro-organisms • Inform patient that fluid loss can lead to a drop in blood pressure that may cause dizziness upon standing and on exertion
Follow-Up	• Patients to be reassessed within 24h. If symptoms not resolved, provide further recommended strategies and arrange stool analysis as indicated. Repeat follow-up assessment within 24h • Instruct patient/family to call back if symptoms worsen or do not improve • If indicated, arrange for nurse initiated telephone follow-up or physician follow-up

Persistent GRADE 1 - GRADE 2
Diarrhea NOT resolving after 24 hours
(no fever, dehydration, neutropenia and/or blood in stool)

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URGENT:
Requires medical attention within 24 hours

Patient Care and Assessment	• Collaborate with physician: – To rule out other causes or concomitant causes of diarrhea or need for further assessment in outpatient setting If patient has Grade ≥ 2 diarrhea, treatment delays or reductions may be required – Refer to specific chemotherapy protocols for direction. ***See Chemotherapy Protocols in Resources Section*** – Lab tests that may be ordered: - Complete blood count (CBC), electrolyte profile, BUN/creatinine - Stool analysis – C. difficile toxin assay, culture and sensitivity (Salmonella, E. coli, Campylobacter, infectious colitis), ova and parasites, blood and leukocytes
Dietary Management	• Consider trial of limiting lactose-containing products to see if symptoms improve • If patient unable to tolerate adequate oral daily fluid intake IV hydration to replace lost fluid and electrolytes may be required
Pharmacological Management	• Avoid/discontinue any medications that may cause or exacerbate diarrhea in collaboration with physician and pharmacist • Medications that may be prescribed: - Loperamide: may be continued at a higher dose or frequency (4mg followed by 2mg every 2h (or 4 mg every 4h at night) until 12h without a loose bowel movement), or discontinued

	and replaced by another antidiarrheal medication - Corticosteroids (Refer to SCIMMUNE if patient is on checkpoint inhibitors) - Refer to SCCRS if patient is on bispecific antibodies - Diphenoxylate - Atropine (Lomotil®) – Octreotide (subcutaneous) – Oral antibiotics if infection suspected (e.g. ciprofloxacin, metronidazole, vancomycin,)* not generally recommended for RT-induced diarrhea

GRADE 3 or 4 Diarrhea

OR

Persistent Grade 1 or 2 diarrhea with one or more of the following symptoms: T ≥ 38° C, abdominal cramping, nausea and vomiting, sepsis, neutropenia, blood in stool, dehydration

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EMERGENT:

Requires IMMEDIATE medical attention

Patient Care and Assessment	• Patients will generally require hospital admission. Notify physician of assessment, facilitate arrangements as necessary • If patient is on checkpoint inhibitor, remind patient to present Immunotherapy Alert Card and patient letter • If patient is on bispecific antibodies, remind patient to present Bispecific Antibodies Alert Card and patient letter • Collaborate with physician: – To rule out other causes or concomitant causes of diarrhea – To hold chemotherapy until symptoms resolve. Chemotherapy may then be restarted at a reduced dose. Refer to specific chemotherapy protocols for direction ***See BC Cancer Chemotherapy Protocols*** • Lab tests that may be ordered: - Complete blood count (CBC), electrolyte profile, BUN/creatinine – Stool analysis – C. difficile toxin assay, culture and sensitivity (Salmonella, E. coli, Campylobacter, infectious colitis), ova and parasites, blood and leukocytes • Nursing Support: – Monitor vital signs as clinically indicated – Record intake and output and daily weight – Pain and symptom assessment and management as appropriate
Dietary Management	• IV hydration to replace lost fluids and electrolytes • Patients may require bowel rest and be NPO • Enteral or parenteral nutrition (TPN) may be indicated
Pharmacological Management	▪ Avoid/discontinue any medications that may cause or exacerbate diarrhea in collaboration with physician and pharmacist ▪ Medications that may be prescribed: – Octreotide (subcutaneous or IV) – Antibiotics (oral or intravenous route) – Systemic analgesia – Corticosteroids (Refer to SCIMMUNE if patient on checkpoint inhibitors – DO NOT administer corticosteroids if bowel perforation is suspected / confirmed) – Refer to SCCRS if patient is on bispecific antibodies

RESOURCES & REFFERALS

Referrals	• Patient support center or telephone care management • Pain and Symptom Management/Palliative Care (PSMPC) • Oncology Nutrition Services (Dietitian) • Home Health Nursing
Management Guidelines	• BC Cancer Guidelines for Chemotherapy-Induced Diarrhea: http://www.bccancer.bc.ca/nursing-site/Documents/GuidelinesforManagementofCID.pdf • Medical Management of Malignant Bowel Obstruction: http://www.bccancer.bc.ca/family-oncology-network-site/Documents/MedicalManagementofMalignantBowelObstruction.pdf
Patient Education	• CDiff and VRE pamphlets (H:\EVERYONE\Infection Control\PAMPHLETS) • http://www.bccancer.bc.ca/health-info/coping-with-cancer/nutrition-support • Coping with Cancer - Diarrhea: http://www.bccancer.bc.ca/health-info/coping-with-cancer/managing-symptoms-side-effects/diarrhea-caused-by-medications • NCI Managing Chemotherapy Side Effects: https://www.cancer.gov/publications/patient-education/diarrhea.pdf • NCI Managing Radiation Therapy Side Effects – What to do When you Have Loose Stools: https://www.cancer.gov/publications/patient-education/radiation-side-effect-diarrhea.pdf • Canadian Cancer Society – Diarrhea: http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/managing-side-effects/diarrhea/?region=on • ASCO Cancer.Net – Diarrhea: https://www.cancer.net/navigating-cancer-care/side-effects/diarrhea
Irinotecan	• Monograph: http://www.bccancer.bc.ca/drug-database-site/Drug%20Index/Irinotecan_monograph.pdf • Patient handout: http://www.bccancer.bc.ca/drug-database-site/Drug%20Index/Irinotecan_handout.pdf
Immunotherapy – Checkpoint Inhibitors	• Immunotherapy Nursing Process • Immunotherapy Patient Letter • Immunotherapy Alert Card • SCIMMUNE protocol • SCIMMUNE patient handout
Immunotherapy - Bispecific Antibodies	• Bispecific Antibodies Nursing Process • Bispecific Antibodies Patient letter • Bispecific Antibodies Alert Card • SCICANS protocol • SCCRS protocol
Alert Guidelines	H:\EVERYONE\nursing\REFERENCES AND GUIDELINES\Telephone Nursing Guidelines\Alert Guideline(available to internal BCCA staff only): • Intestinal Obstruction
Bibliography List	• http://www.bccancer.bc.ca/nursing-site/Documents/Bibliograpy%20-%20Master%20List.pdf

Appendix

Contributing Factors	
Cancer Related	• Colon • Neuroendocrine tumors (e.g. VIPomas, carcinoid, gastrinomas) • Lymphoma • Pancreatic • Pheochromocytoma • Graft vs. host disease after bone marrow transplant
Treatment Related	**Systemic Treatment:** • Capecitabine • 5 – fluorouracil • Irinotecan • Leucovorin • Most small molecule oral tyrosine kinase inhibitors (TKIs) • Immunotherapy – Checkpoint inhibitors • Immunotherapy - Bispecific Antibodies: Diarrhea may be a symptom of cytokine release syndrome (CRS) • Biotherapy (e.g. high dose Interferon or Interleukin– 2) **Radiation Treatment Fields:** • Pelvic • Abdominal • Lumbar • Para-aortic fields • Lung • Head and neck **Surgical Treatment:** • Celiac plexus block • Large or small bowel resection • Cholecystectomy, esophagogastrectomy • Gastrectomy, pancreaticoduodenectomy (Whipple procedure) • Vagotomy • Terminal ileal resection and loss of ileocecal valve
Medications and Supplements	• Laxatives (e.g. stool softeners, stimulant laxatives) • Antibiotics (e.g. cephalexin, amoxicillin, clindamycin, clavulanic acid-amoxicillin) • Prokinetic agents (e.g. metoclopramide, methyldopa, cochicine, digoxin) • Antihypertensives • Misoprostol • Potassium supplements • Magnesium-containing antacids / supplements • Liquid medications containing sorbitol (e.g. acetaminophen elixir) • Caffeine • Alcohol • Herbal supplements (e.g. milk thistle, aloe, cayenne, saw palmetto, ginseng, coenzyme Q10, high dose vitamin C)

Medical History	
	• Partial bowel obstruction, fecal impaction with overflow • Obstruction of common bile duct • Inflammatory bowel disease (e.g. Crohn's disease, ulcerative colitis) • Irritable bowel syndrome, diverticulitis, ischemic colitis • Narcotic withdrawal • Diabetes • Hyperthyroidism • Hypoalbuminemia • Conditions that may require use of warfarin (e.g. venous thrombosis, cardiac surgeries) • Advanced age • Anxiety, stress • Recent travel • Infection- viral (e.g. norovirus), bacterial (e.g. C.difficile, E.coli), parasitic • Post-pyloric hyperosmolar feedings and/or high feeding rate • Food/ lactose intolerance

Consequences

- Dehydration and electrolyte imbalances, cardiovascular compromise and neurological compromise
- Weight loss, malnutrition and cachexia
- Infection, sepsis
- Chemotherapy dose delays, reductions, discontinuation of treatment
- Decreased quality of life – distress, fatigue, compromised role function, decreased functional status, exacerbation of other symptoms
- Diarrhea may result in increased INR, or increased risk of bleeding for patients on warfarin

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