

Preventing and Treating Diarrhea Related to Chemotherapy and/or Radiation Therapy

Systematic Review/Meta-analysis Table

(Literature search completed through May 2008)

Review Author	Study Information	Conclusions and Implications
<b>Recommended Guidelines for the Treatment of Cancer Treatment-Induced Diarrhea</b>		
<p>Benson, et al. 2004</p>	<p>An expert multidisciplinary panel convened to review recent literature            Search strategy: MEDLINE of relevant literature since 1998, year of previous guideline publication; also expert opinion plus unpublished data from completed or ongoing studies            Panel composition: 11 academic practitioners with backgrounds in med oncology, radiation oncology, BMT, gastroenterology, and endocrinology            Key search terms: radiation, chemotherapy, diarrhea, octreotide, and somatostatin analog</p>	<p>Recommended for practice for the treatment of chemotherapy-induced diarrhea (CID). Loperamide (4 mg initial dose followed by 2 mg every 4 hours) is recommended as the standard first-line therapy for CID</p> <ul style="list-style-type: none"> <li>• High-dose loperamide (2 mg every 2 hours) has been shown to be moderately effective in the control of CID associated with irinotecan</li> <li>• Somatostatin analog, octreotide acetate, at a standard dose of 100 to 150 micrograms three times daily via the SC route is recommended for uncontrolled NCI grade 1 or 2 CID or for grade 3 or 4 CID</li> </ul> <p>Recommended for practice for the treatment of radiation-induced diarrhea</p> <ul style="list-style-type: none"> <li>• Oral opiates, including loperamide and diphenoxylate, are effective in the majority of patients with mild symptoms and are the standard therapy.</li> <li>• Octreotide 100 micrograms SQ three times daily is more effective than diphenoxylate 10 mg po per day in patients with grade 2 or 3 diarrhea</li> </ul> <p>Effectiveness not established for the treatment of CID</p> <ul style="list-style-type: none"> <li>• Upward titration of octreotide from 150 micrograms up to 500 micrograms three times daily SC until symptoms are controlled may be more effective than standard doses in patients with CID who fail loperamide.</li> </ul> <p>Effectiveness not established for the prevention CID</p> <ul style="list-style-type: none"> <li>• Strategies for the prevention of irinotecan-induced diarrhea require further investigation</li> </ul> <p>Effectiveness unlikely for the prevention of radiation-induced diarrhea</p> <ul style="list-style-type: none"> <li>• Until a confirmatory trial is conducted, sulfasalazine should not be used outside of a clinical trial in patients receiving pelvic radiation therapy</li> </ul> <p>Not recommended for practice for prevention of radiation-induced diarrhea</p> <ul style="list-style-type: none"> <li>• Sucralfate is not effective in preventing radiation therapy-induced diarrhea and may aggravate some gastrointestinal symptoms</li> </ul> <p>Expert opinion for CID</p> <ul style="list-style-type: none"> <li>• A high degree of vigilance is needed with regard to monitoring GI toxicity for patients receiving irinotecan-based therapy and other intensive combination regimens</li> <li>• Assessment of symptoms needs to be rigorous and should include duration of symptoms, constellation of signs and symptoms, and severity of symptoms               <ul style="list-style-type: none"> <li>○ Assess number of stools over baseline and stool composition, including presence of nocturnal diarrhea</li> <li>○ Assess presence of added risk factors: fever, orthostatic symptoms (e.g.,</li> </ul> </li> </ul>

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		<p>dizziness), abdominal pain or cramping, or weakness</p> <ul style="list-style-type: none"> <li>○ Stool volume, although a valuable piece of information, may be impractical to determine</li> <li>○ Assess hydration status by physical examination</li> <li>○ Assess dietary intake for diarrhea-enhancing foods. Eliminate lactose containing foods, alcohol, and high osmolarity foods or beverages. Increase clear liquid consumption (e.g., Gatorade, broth) to at least 8–10 glasses per day and consume small, frequent meals with low-fiber, starchy foods such as bananas, rice, toast or pasta.</li> </ul> <ul style="list-style-type: none"> <li>• Patients with grade 3 or 4 CID or with grade 1 or 2 CID and added risk factors as stated above should have a stool work-up (evaluation for blood, fecal leukocytes, <i>C difficile</i>, <i>Salmonella</i>, <i>E coli</i>, <i>Campylobacter</i>, and infectious colitis), complete blood count, and electrolyte profile</li> <li>• Tincture of opium is a widely used anti-diarrheal agent and may be a reasonable alternative as second-line therapy for CID. Two preparations are available and because of the difference in morphine content, care must be taken not to confuse them       <ul style="list-style-type: none"> <li>○ Deodorized tincture of opium, the preferred preparation, contains the equivalent of 10 mg/ml morphine. The recommended dose is 10 to 15 drops in water every three to four hours.</li> <li>○ Camphorated tincture of opium (paregoric), a less-concentrated preparation, contains the equivalent of 0.4 mg/ml morphine. The recommended dose is 1 teaspoon (5 ml) in water every three to four hours.</li> </ul> </li> </ul>
<p><b>Recommended Guidelines for the Use of Glutamine Supplementation for Prevention and Treatment of Cancer Treatment-Induced Diarrhea</b></p>		
<p>Savarese et al. 2003</p>	<p>A meta-analysis of literature on human and animal studies of glutamine use in subjects with cancer.</p> <p>Authors searched MEDLINE database 1980–2003 as well as manually searching bibliographies of published articles for relevant references.</p> <p>Evaluated evidence of effect of glutamine supplementation on toxicities resulting from chemotherapy and radiation therapy, also discussed potential effect of glutamine on enhancing carcinogenic process (i.e., making tumor cells more sensitive to treatment)</p>	<p>Glutamine supplementation may decrease the incidence and/or severity of irinotecan-associated diarrhea; inconclusive evidence regarding effect on radiation-induced diarrhea</p> <p>Limitations: Examines multiple toxicities, therefore not specific to effect on incidence/severity of diarrhea.</p> <p>Strengths: Causal mechanism identified for both how glutamine protects GI tract and prevent diarrhea and for the etiology of enhanced tumor sensitivity to glutamine</p> <p>Glutamine powder (not tablets) is inexpensive and able to be added to any liquid or solid food product.</p> <p>The beneficial effects of glutamine are seen whether administered parenterally or enterally.</p> <p>Specific dose recommendation: 30 g per day. Recommendation is based on usual PO consumption of 10 g per day on western diet versus increased need during metabolic stress/catabolic insult such as cancer progression and treatment (increased need cited as 20–40 g per day)</p>



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<b>Recommended Guidelines for the of Use of Selenium for Treatment of Radiation-Induced Diarrhea</b>		
Dennert & Horneber, 2006	Selenium for alleviating side effects of chemotherapy, radiotherapy, and surgery in patients with cancer  Search category: Cochrane Database	No evidence selenium supplements reduce side effects of chemotherapy, RT, or effects of surgery in patients with cancer. One RCT for radiation-induced diarrhea; none in this review for chemotherapy-related diarrhea
<b>Recommended Guidelines for the Use of Psyllium Fiber for the Treatment of Diarrhea</b>		
Singh, 2007	A review article on the use of psyllium for multiple conditions/disease states, including diarrhea caused by food, chemical laxatives, drugs (such as antibiotics) and infection. Search terms and databases searched are not disclosed in publication.  Note: Author does not specifically address diarrhea resulting from cancer treatment	Psyllium (a soluble fiber) adds bulk to stools, thereby increasing the number of normal stools and decreasing the number of liquid stools. Psyllium also has been found to increase intestinal transit time by delaying gastric emptying.  Psyllium use is associated with decreased episodes of diarrhea in children with non-specific chronic diarrhea, decreased percentage of incontinent stools, and an improvement in stool consistency among patients with irritable bowel syndrome .
<b>Recommended Guidelines for the Use of Probiotics for the Treatment of Diarrhea</b>		
Marteau et al., 2001	A review article on the use of probiotics for multiple gastrointestinal diseases, including radiation-induced diarrhea, antibiotic-associated diarrhea, gastroenteritis, traveler's diarrhea, and inflammatory bowel disease. Search terms and databases searched are not disclosed in publication.	The authors cite open trials of freeze-dried lactic acid bacteria cultures for the treatment of radiation-induced diarrhea, as well as one randomized controlled study, which found a significant decrease in diarrhea when <i>L. acidophilus</i> NDCO 1748 was administered during pelvic irradiation.  The authors conclude that further studies are needed to confirm probiotics as a potential therapeutic intervention for the treatment of diarrhea during pelvic irradiation.