The Prophylactic Use of Probiotics in the Prevention of Radiation Therapy-Induced Diarrhea

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Cancer treatment regimens that include radiation therapy (RT) to the abdominal region for cervical, ovarian, prostate, sigmoid, or colorectal cancer potentially disturb the colonization resistance of the indigenous gut flora, causing RT-induced diarrhea, enteritis, and colitis in more than 80% of patients with cancer. One approach for the prevention of RT-induced diarrhea is the use of probiotics. Randomized clinical trials have demonstrated efficacy of probiotic preparations VSL #3 and *Lactobacillus casei* DN-114 001 in decreasing the incidence and grade of RT-induced diarrhea. Oncology nurses and advanced practice clinicians are in a position to interpret research findings related to RT-induced diarrhea, enteritis, and colitis and to apply evidence-based practice principles in patients with cancer receiving RT to promote positive outcomes.

Radiation therapy (RT) treatment regimens focused on the abdominal and pelvic region for cervical, ovarian, prostate, sigmoid, or colorectal cancer have the potential to disturb the colonization resistance of the indigenous gut flora. Disruption of colonization resistance is the main pathophysiologic mechanism of acute RT-induced enteritis and colitis, a common and often severe complication among patients with cancer receiving RT (Delia et al., 2007) (see Figure 1). The gut is a complex microbial ecosystem that consists of three basic components: microflora, host cells, and ingested food (Blanarova, Galovicova, & Petrasova, 2009). The gut contains an estimated 60%–80% of the immune system's components (Minocha, 2009). Disruption of this ecosystem alters the host's homeostasis, contributes to intestinal injury, and prevents healing (Giralt et al., 2008). Despite the success of abdominal and pelvic RT in treating tumors, it has adverse effects. More than 80% of patients receiving abdominal or pelvic RT will experience adverse effects that include diarrhea, nausea, and vomiting. As Giralt et al. (2008) noted, diarrhea is not only the most frequently reported adverse effect of RT, but it also causes the most distress.

Acute radiation enteritis is defined as an inflammatory and degenerative process that affects all components of the gastrointestinal tract and can occur as early as five to eight days after RT doses of 8 Gy or more (Blanarova et al., 2009). The pathogenesis of RT-induced enteritis includes DNA damage, expression of adhesive molecules in the gastrointestinal tract, decelerated mitotic activity in the cryptal epithelium, denudation of the basal membrane, and micro-ulcerations (Blanarova et al., 2009). These changes lead to cryptal and villi atrophy along with cellular necrosis. Functional changes in the intestinal mucosa which lead to diarrhea include the malabsorption of lactose and bile acids, altered composition of intestinal flora, and changes in the structure of intestinal motility resulting in impaired secretion, absorption, and immune function of the digestive tract (Blanarova et al., 2009; Giralt et al., 2008).

At a Glance

✦ Radiation therapy (RT) to the abdominal and pelvic region can cause RT enteritis, a gastrointestinal tract inflammatory process that leads to severe diarrhea.

✦ Probiotics such as VSL #3 and *Lactobacillus casei* DN-114 001 have demonstrated efficacy in reducing the incidence and severity of diarrhea from RT enteritis.

✦ Oncology nurses and advanced practice clinicians are instrumental in providing patients with evidence-based information on the use of probiotics to decrease diarrhea.

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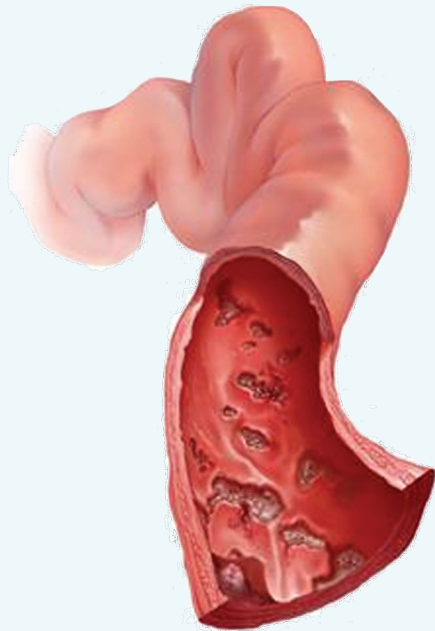
Figure 1. Pathological Changes in the Small Bowel From Radiation Therapy Enteritis

Note. From "CT of Non-Neoplastic Disease of the Small Bowel: Spectrum of Disease," by K. Horton, F. Corl, and E. Fishman, 1999, *Journal of Computer Assisted Tomography, 23,* p. 420. Copyright 1999 by Wolters Kluwer. Reprinted with permission.

RT-induced diarrhea is treated with antibiotics, sucralfate, anti-inflammatory medications such as mesalazine and balsalazide, glutamine, octreotide, proteolytic enzymes, and hyperbaric oxygen (Delia et al., 2007; Muehlbaur & Thorpe, 2009). Treatment failure occurs in a substantial proportion of patients, although exact statistics are not reported (Giralt et al., 2008; Muehlbaur & Thorpe, 2009).

Innovative approaches that target other mechanisms in the pathophysiology of RT-induced diarrhea are needed. One possibility is the use of probiotics. Probiotics are products or preparations that contain viable and defined microorganisms such as *Lactobacillus* and *Bifidobacterium* in a quantity sufficient to alter the host's microflora by implantation or colonization and maintenance of the balance between pro-inflammatory and anti-inflammatory cytokines (Balanarova et al., 2009; Reid, Sanders, et al., 2003).

Although the probiotic concept has been discussed for almost a century, only recently have the tools become available to properly evaluate the effects of probiotics on normal health and well-being and their potential in preventing and treating disease (Reid, Sanders, et al., 2003). A number of studies have provided insight regarding the effect of probiotics on growth and metabolic influences (Delia et al., 2007; Giralt et al., 2008; Reid, Sanders, et al., 2003). Delia et al. (2007) compared the commercially available probiotic preparation known as VSL #3 (VSL Pharmaceuticals) with a placebo in the treatment of RT–induced diarrhea in 490 patients undergoing adjuvant RT for sigmoid, rectal, or cervical cancers. A higher incidence of RT-induced enteritis and colitis was noted in the placebo group than in the VSL #3 treatment

group (51.8% versus 31.6%, p < 0.001). The number of daily bowel movements was significantly reduced in the probiotic group, as was the grade of diarrhea.

Patients with cancer experiencing diarrhea report feeling fearful, embarrassed, and uncertain (Savard & Sawatzky, 2007). By virtue of their comprehensive understanding of the human response to illness, oncology nurses and advanced practice clinicians (APCs) are in a unique position to address patients' concerns and institute individualized, evidence-based management strategies, which may include the use of probiotics (Savard & Sawatzky, 2007). The purpose of this evidentiary review is to explore the use of probiotics in preventing, reducing, and managing RT-induced diarrhea.

Background and Significance

Detailed information on the genetics of lactic acid bacteria is now known because of the availability of sophisticated genetic, microbiologic, and bioinformatic tools. The incorporation of these tools into a multidisciplinary scientific platform is expected to clarify the contributions of probiotics to a patient's general health and well being and identify specific host responses (Reid, Sanders, et al., 2003).

Probiotics perform by secreting antimicrobial substances such as hydrogen peroxide, organic acids, and bacteriocins, which make the intestinal luminal environment hostile to aggressive bacteria (Savard & Sawatzky, 2007). Probiotics occupy the limited physical space in the mucosal layer of the gut, thereby replacing pathogenic microorganisms (Blanarova et al., 2009; Savard & Sawatzky, 2007). Probiotics induce intestinal production of anti-inflammatory cytokines and reduce the production of pro-inflammatory cytokines (Blanarova et al., 2009; Savard & Sawatzky, 2007). Most probiotics belong to a group of lactic-acid producing bacteria (lactobacilli, streptococci, and bifidobacteria), which are part of the normal intestinal microflora (Blanarova et al., 2009; Savard & Sawatzky, 2007). Each probiotic strain induces lymphocytes, enterocytes, or dendritic cells to produce unique cytokines (Minocha, 2009). Several mechanisms that may explain how lactobacilli reduce the duration of diarrhea have been proposed (Reid, Jass, Sebulsky, & McCormick, 2003). Lactobacilli competitively block intestinal receptor sites and enhance the immune response. They also may decrease intestinal secretion, intestinal motility, and inactivate viral particles (Reid, Jass, et al., 2003). Additional research is needed to understand how probiotic strains reduce the duration of diarrhea in conjunction with rehydration therapy and may lead to a better understanding of the disruption of the dynamics of the intestinal microbiota that are associated with rapid fecal loss (Reid, Jass, et al., 2003).

The use of probiotics as therapeutic agents for gastrointestinal disorders is gaining wider attention (Fedorak & Madsen, 2004). Probiotics exert protective functions through the modulation of immune activity and epithelial function in the small and large intestine. Immune and epithelial cells can discriminate between different microbial species through activation of toll-like receptors (Fedorak & Madsen, 2004). This ability to differentiate immune activity and epithelial function has led to increased credibility for the use of probiotics in clinical medicine (Fedorak & Madsen, 2004).

Current clinical experience with probiotic organisms for the prevention of enteritis and colitis in patients with cancer receiving RT is limited (Delia et al., 2007). The probiotics *Lactobacilli* and *Bifidobacteria* have both been used in food products and dietary supplements for decades, with a compelling record of safe consumption. Preliminary data suggest that probiotic intervention may be useful in inflammatory bowel disease, irritable bowel syndrome, allergy, colorectal cancer (75% of colorectal cancers are associated with diet [Reid, Sanders, et al., 2003]), vaginal and urinary tract infections in women, kidney stone disease, mineral absorption, and infections caused by *Helicobacter pylori* (Reid, Sanders, et al., 2003). Evidence also suggests that the metabolites of certain gut microbes impact conditions ranging from coronary heart disease to cognitive dysfunction, suggesting the possibility that probiotics may be a useful intervention in these entities as well (Reid, Sanders, et al., 2003).

Educating patients and their families about pharmacologic and complementary or alternative interventions helps foster positive and beneficial responses to illness. Knowledge facilitates self-management and enables patients to complete the RT regimen (Savard & Sawatzky, 2007). Many consumers and healthcare professionals have limited knowledge regarding probiotics or are completely unfamiliar with the different strains of probiotic organisms and their benefits. Considerable differences also exist among probiotic preparations with regard to bioavailability, biological activities, doses, and composition (Tamayo, 2008). With these factors in mind, oncology nurses and APCs can provide information about probiotics, the different strains of probiotics available, differences between probiotic preparations, and the potential benefits of use to allow the patient to make an informed choice (Oncology Nursing Society [ONS], 2007; Tamayo, 2008). Although probiotics are not curative therapy, they represent a valuable adjunctive agent when used appropriately (Savard & Sawatzky, 2007).

Review of Literature

To address the question of whether the prophylactic use of probiotics is effective in preventing RT-induced diarrhea, a review was conducted of literature published from 2002–2009. PubMed, Ovid, and the Cochrane collection of databases were searched using the following key terms alone and in combination: *probiotic*, *radiation therapy*, *diarrhea*, *radiation therapy-induced diarrhea*, *gastrointestinal disorders*, and *prevention*. The six studies (evidence levels ranged from II [evidence obtained from at least one randomized controlled trial] to VII [evidence from the opinion of authorities or expert committees]) most directly applicable to the question of probiotic use and RT-induced diarrhea were included for review.

Delia at al. (2007) conducted a double-blind, randomized clinical trial (RCT) to investigate the efficacy of a high-potency probiotic preparation on prevention of RT-induced diarrhea in patients with cancer. Patients (N = 490) who underwent adjuvant postoperative radiation therapy after surgery for sigmoid, rectal, or cervical cancer were randomized to either the high-potency probiotic preparation VSL #3 (one sachet three times per day) (n = 243), or to the placebo group who received an iden-

tical appearing sachet (three times per day) (n = 239) beginning on the first day of RT. The primary outcomes considered were incidence and severity of RT-induced diarrhea, daily number of bowel movements, and the number of days of loperamide use as a rescue medication (Delia et al., 2007). Patients in the placebo group (51.8%, p < 0.001) reported significantly more RT-induced diarrhea than the patients in the VSL #3 group (31.6%; p < 0.001). More patients in the placebo group suffered grade 3 or 4 diarrhea compared with VSL #3 recipients (55.4% and 1.4%, p < 0.001, respectively). The mean number of daily bowel movements was 14.7 (SD = 6) in the placebo group and 5.1 (SD = 3) among the VSL #3 recipients (p < 0.05). The mean time to the use of rescue dose loperamide was 86 (SD = 6) hours for the placebo group and 122 (SD = 8) hours for the VSL #3 group (p < 0.001) (Delia et al., 2007). Delia et al. (2007) concluded that the use of a probiotic made a dramatic difference in reducing the frequency and severity of diarrhea.

Fedorak and Madsen (2004) summarized the clinical efficacy of probiotics in patients with gastrointestinal disorders and examined the mechanism of action of probiotics (level VII evidence) and found that immune and epithelial cells discriminate between different microbial species through the activation of toll-like receptors. This indicates that probiotics may exert some of their protective functions through the modulation of immune activity and epithelial function in the small and large intestine.

Delia et al. (2002) conducted a double-blind RCT in which the efficacy of VSL #3 to prevent RT-induced diarrhea in 95
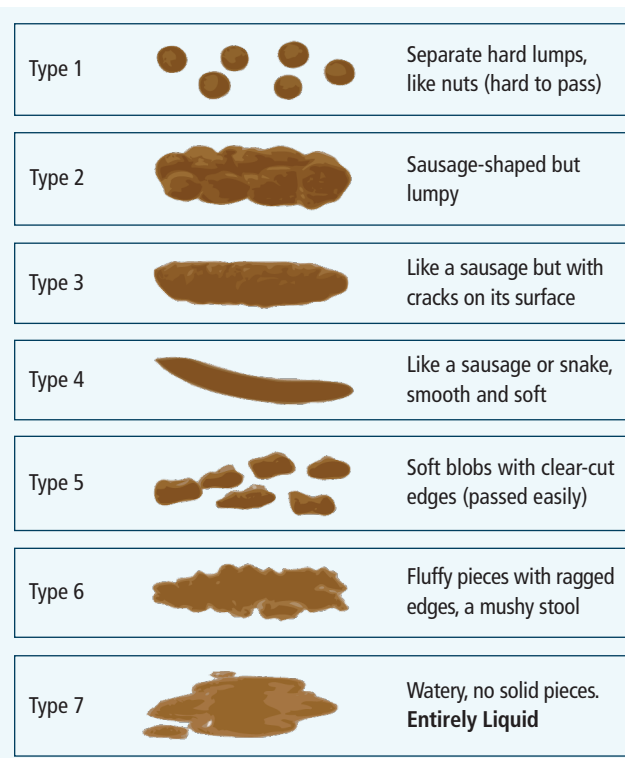

Figure 2. Bristol Stool Chart

Note. From "Stool for Scale as a Useful Guide to Intestinal Transit Time," by S.J. Lewis and K.W. Heaton, 1997, *Scandinavian Journal of Gastroenterology, 32,* p. 921. Copyright 1997 by Informa Healthcare. Reprinted with permission.

Table 1. Common Terminology Criteria for Adverse Events, Version 4: Gastrointestinal Disorders

ADVERSE EVENT	GRADE				
	1	2	3	4	5
Diarrhea: a disorder characterized by frequent and watery bowel movements.	Increase of less than four stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of four to six stools per day over baseline; moderate increase in ostomy output compared to baseline	Increase of greater than or equal to seven stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limited self-care activities of daily living	Life-threatening consequences; urgent intervention indicated	Death

Note. From "Common Terminology Criteria for Adverse Events, Version 4" by the U.S. Department of Health and Human Services, 2009. Retrieved from http://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/ctcaev4.pdf

patients undergoing pelvic radiation was evaluated. Patients in the placebo group (n = 95) had more RT-induced diarrhea (55%) compared with those in the VSL #3 group (n = 95) (38%) (p < 0.001). Patients in the placebo group had 12.3 (SD = 4) daily bowel movements compared with 4.6 (SD = 2) in the VSL #3 group (p < 0.05), and 97 (SD = 4) hours until the use of loperamide as a rescue agent compared to 118 (SD = 6) hours until use of loperamide in the VSL #3 group (p < 0.001) (Delia et al., 2002).

Giralt et al. (2008) conducted a double-blind RCT to determine whether a probiotic drink containing *Lactobacillus casei* DN-114 001 reduced the incidence of RT-induced diarrhea in patients with gynecologic cancer. Eighty-five patients undergoing pelvic radiotherapy (45–50 Gy, conventional fractionation) for either cervical carcinoma or endometrial carcinoma were randomly assigned to a yogurt drink containing *L. casei* DN-114 001 or liquid yogurt placebo. Patients recorded their number of bowel movements and scored stool consistency using the seven-point Bristol Stool Chart (see Figure 2). The Bristol Stool Chart is a useful tool for patients, oncology nurses, and APCs to use to correctly classify stool by consistency. The diarrhea was graded on a weekly basis using the Common Toxicity Criteria for Adverse Events [v.4.0] (CTCAE) (Giralt et al., 2008; U.S. Department of Health and Human Services, 2003) (see Table 1). The primary endpoint in this study was to reduce the incidence of diarrhea, as defined by a CTCAE grade of 2 or greater or the need for loperamide. Grade 2 diarrhea is defined as four or more bowel movements per 24 hours.

Results demonstrated that diarrhea of grade 2 or greater and/or the use of loperamide was observed in 24 of 41 patients (58.5%) in the placebo group and 30 of 44 patients (68%) in the probiotic group (p = 0.57). No differences were found in the median time to the presentation of grade 2 or greater diarrhea or the need for loperamide. Probiotic intervention did, however, have a significant effect on stool consistency (p = 0.04), which was assessed using the Bristol Stool Chart. The Bristol Stool Chart assessment ranged from type 1 (separate hard lumps) to type 7 (entirely liquid). The median time for patients to present with Bristol Stool Chart stools of type 6 or greater was 14 days for patients who received the probiotic drink and 10 days for patients receiving the placebo (p = 0.05) (Giralt et al., 2008).

Recommendations for probiotic use in RT-induced diarrhea were described by Floch et al. (2008). These recommendations were based on studies presented at the Advances in Clinical Use of Probiotics Workshop at Yale University in November 2007

(level VII evidence). The use of probiotics in the prevention of RT-induced diarrhea received a "C" recommendation, which is defined as incorporating some positive studies. This recommendation level was assigned based on the limited number of studies on probiotic use in the prevention of RT-induced diarrhea and small sample sizes (Floch et al., 2008). More level II evidence RCTs are required to evaluate the safety and efficacy of specific probiotics prior to upgrading the recommendation.

Probiotics

An expert panel report from the United Nations (UN) and the World Health Organization (WHO) defined probiotics as live microorganisms that confer a health benefit in the host when administered in adequate amounts (Reid, 2008). Subsequent guidelines published by the UN and WHO were endorsed by the International Scientific Association for Probiotics and Prebiotics. These guidelines provide clinical, scientific, and manufacturing standards that must be met for products to be called "probiotic." The guidelines also serve as a resource for developing new strains and new applications for probiotics. According to Reid (2008), these advances will lead to new breakthroughs in probiotic use through studies on the origin of microbiota, dietary factors, disease processes, infectious biofilm formation, and delivery mechanisms of probiotics.

The use of hypoglycemic agents and dietary modification in the management of diabetes is an example of a pharmaceutical and dietary intervention that has fundamentally altered the course of a disease. The prophylactic use of probiotics in the prevention of RT-induced diarrhea may have a similar effect on the quality of life of patients with cancer. Biomedical engineering advances, such as encasing of probiotics in nanoaggregates that protect against stomach acid and the encapsulation of probiotics to rehydrate at specific sites, are examples of contributions to developing systems that deliver bacteria and/or nutritional factors to the host (Reid, 2008). At the macromolecular level, coating capsules with biosensors that detect the optimal conditions for the release of probiotic contents will soon be possible, and recombinant strains that respond to specific triggers in a host (e.g., a toxin) and produce factors to counteract them are in development (Reid, 2008).

Current research is focusing on a multitude of organisms, diverse delivery vehicles, and potential health targets such that

general conclusions cannot be reached. The incorporation of genetic tools within a multidisciplinary scientific platform is expected to reveal the contributions of probiotics and prebiotics to general health and well being and explicitly identify the mechanisms and corresponding host responses that provide the basis for their positive roles and associated claims (Reid, Sanders, et al., 2003). Although encouraging, additional evidence is needed to evaluate the efficacy of probiotics in the prevention of RT-induced diarrhea.

Safety and Potential Complications of Probiotic Therapy

As probiotics are viable organisms, they may infect the host. Although data have indicated that the probiotics *Lactobacilli* and *Bifidobacteria* are safe for human use, side effects have been reported that include rare systemic infections (Reid, Jass, et al., 2003). A need exists for additional precautions when administering live bacteria to immunocompromised patients and those with intestinal bleeding. Caution must be exercised to ensure that excessive stimulation of the immune system is not induced in patients who are susceptible to the development of arthritis and other autoimmune conditions (Reid, Jass, et al., 2003). Additional considerations in probiotic administration must include potential contraindications, a proven history of safe use for the dose and administration route, and frequency of infection with the probiotic strain (Reid, Jass, et al., 2003). The concept of safety becomes more important if one considers organisms such as *Enterococcus* as probiotics (Reid, Jass, et al., 2003). These bacteria are present in high numbers in the intestine, and often are included in probiotic cocktails. However, enterococci have become an increasingly important cause of vancomycin-resistant nosocomial infections (Reid, Jass, et al., 2003). *Saccharomyces boulardii* is another organism that is widely used as a probiotic, yet also has been associated with fungemia (Reid, Jass, et al., 2003).

To establish safety guidelines for probiotic organisms, the Food and Agricultural Organization of the UN (FAO) and the WHO have recommended that probiotic strains be characterized using a series of tests that include antibiotic-resistance patterns, metabolic activities, toxin production, hemolytic activity, infectivity in immunocompromised models, side effects in humans, and adverse incidents in consumers (Reid, Jass, et al., 2003). Specific health claims and labeling are necessary to better inform the user of the benefits of the product (Reid, Jass, et al., 2003). An additional implication of the FAO/WHO definition is that, unless strains demonstrate clinically established physiologic benefits, they should not be referred to as probiotics (Reid, Jass, et al., 2003). In vitro testing cannot be assumed to predict functionality in the human body and are not sufficient to substantiate the use of the term probiotic (Reid, Jass, et al., 2003).

Health Policy

The Food, Drug, and Cosmetic (FDC) Act lays out a legal framework that governs products including probiotics. The degree of restraint that can be imposed on a product depends on how the product is categorized for intended use (Degnan, 2008).

Probiotics meeting the definition of a new drug or biologic product (e.g., VSL #3) are subject to the testing requirements of the investigational new drug (IND) application. These requirements include formal notification to the U.S. Food and Drug Administration (FDA) about the intent to conduct clinical studies, submission of comprehensive test protocols to the FDA, development of an investigation plan, and institutional review board oversight (Degnan, 2008). Detailed product information should be included as part of an IND application; therefore, the submission of such information requires a probiotic manufacturer that is willing to participate in the application process (Hoffman, Heimbach, Sanders, & Hibberd, 2008).

The regulatory categorizations in the FDC Act reflect an intentional attempt by Congress to avoid a one-size-fits-all approach to the regulation of products. Probiotics potentially possess functional benefits beyond those that traditionally accompany dietary supplements, food, or food ingredients. The FDC Act reflects the Congressional judgment that product claims should be subject to increasingly demanding scientific scrutiny and substantiation requirements that depend on the nature and context of the benefit claimed (Degnan, 2008).

Recommendations for the use of probiotics must be driven by availability of reliable products and evidence-based data (Hoffman et al., 2008). Probiotics are a relatively new subject of scientific research and product development and, therefore, need internationally accepted definitions and precise language to describe the products and their impact on health and disease (Hoffman et al., 2008). The U.S. and European probiotic markets are poised for vigorous growth in the upcoming years; however, no international consensus exists regarding the methodology used to assess their efficacy and safety (Tamayo, 2008). To date, the regulatory category in which a probiotic is placed while being studied depends on the regulations within the country of origin, regardless of how the probiotic is marketed (Hoffman et al., 2008). Factors such as regulatory categories, formulation, route, target consumers, and safety dictate which regulations are imposed on the clinical research, development, manufacturing, and marketing processes (Hoffman et al., 2008).

Recommendations for Practice

Oncology nurses and APCs are positioned to participate in clinical and nursing research and to apply evidence-based research to promote positive outcomes for patients with cancer and their caregivers. One of the roles of oncology nurses and APCs is

Table 2. Recommendations for Probiotic Use

PROBIOTIC	INDICATION FOR USE	USUAL DOSE	APPROXIMATE COST PER MONTH
Lactobacillus casei DN-114 001	Prophylaxis of radiation therapy-induced diarrhea	96 ml of 10^8 CFU/g *L. casei* three times per day	$24 for 100 capsules
VSL #3	Prophylaxis of radiation therapy-induced diarrhea	One capsule three times per day	$67.50 for 90 capsules

preplanning to prevent and/or minimize treatment-related side effects such as RT-induced diarrhea. The integration of evidence-based, pharmacologic, and nonpharmacologic treatment modalities, such as probiotic use, may be incorporated into the treatment plan (ONS, 2007). Recommendations regarding initiation of treatment, dosing, frequency, and duration of therapy are contingent on the specific probiotic being used (see Table 2).

Nursing theorist Dorothea Orem's self-care practice model views individuals as responsible for self care in relationship to health. According to Orem, nursing is considered to be a mode of helping, wherein the focus is the individual's self-care action. Nursing intervention is necessary to sustain life and health, to facilitate recovery from disease or injury, and to assist individuals to cope with the effects of such threats to their self-care abilities (Clarke, Allison, Berbiglia, & Taylor, 2009; Whelan, 1984). In using Orem's self-care model, oncology nurses and APCs assess the risk of RT-induced diarrhea in individual patients with cancer. Prompt and effective symptom management is a hallmark of a radiation oncology nurse's care for patients receiving multimodality therapy (Carper & Haas, 2006). Anticipating patients' needs before they arise and ensuring the availability of adequate and effective medications is necessary to minimize treatment breaks. Oncology nurses and APCs collaborate with the patient, family, caregivers, and multidisciplinary team to formulate a comprehensive plan of care which may include the choice of probiotics for the prevention of RT-induced diarrhea (Carper & Haas, 2006).

Both oncology nurses and APCs participate in the implementation of new protocols, develop patient-education materials, and ensure staff competencies (Carper & Haas, 2006). Of particular importance is patient and staff education regarding pharmacologic and complementary or alternative interventions. Patient education also empowers patients, facilitates self-management, and can potentially improve patient outcomes. Oncology nurses and APCs can advocate on the behalf of their patients by discussing probiotics either as an alternative or as a complementary form of therapy, as patients may not be aware that probiotics are available (Savard & Sawatzky, 2007).

Summary and Conclusion

Cancer treatment regimens that include RT to the abdominal region can disturb the colonization of the indigenous gut flora, causing RT-induced diarrhea, enteritis, and colitis in more than 80% of patients. A possible approach in reducing RT-induced diarrhea is the use of probiotics. Several RCTs have demonstrated the efficacy of probiotic preparations VSL #3 and *L. casei* DN-114 001 in decreasing the incidence and grade of RT-induced diarrhea. Future clinical trials are needed to determine the environment origins of our microbiota and which microbiota may be appropriate as delivery mechanisms. Diet and microbes influence the fundamental aspects of immunity and development; however, little is known about how bacteria are acquired and which ones should be supplemented to achieve short- and long-term health goals. Oncology nurses and APCs are in an ideal position to participate in and interpret research findings related to RT-induced diarrhea, enteritis, and colitis, and to apply evidence-based findings for patients with cancer receiving RT.

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