



## The Effect of Probiotics on Radiation Enteritis in Endometrial Cancer Patients Undergoing Radiotherapy

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### ABSTRACT

**Introduction:** Radiation enteritis is damage to the small and large intestines caused by radiation therapy for regional cancer treatment. The incidence is around 90% in patients undergoing radiation in the pelvic and abdominal regions. This study aimed to report the effect of probiotics on radiation enteritis in endometrial cancer patients. **Case presentation:** A 57-year-old morbidly obese woman diagnosed with endometrial cancer underwent chemoradiation therapy. On the 21st out of 25 radiation sessions and the 2nd chemotherapy session, the patient visited the nutrition clinic at the Radiation Oncology Therapy Center with a complaint of diarrhea for the past 5 days. The diarrhea occurred approximately 10 times a day, with each bowel movement being approximately 50 ml and yellow in color. The patient was then treated with anti-diarrheal therapy, probiotics (*Lactobacillus acidophilus*, *Bifidobacterium longum*, and *Streptococcus thermophilus*) 2 times a day, zinc 20 mg once a day, and prescribed a low-fat and lactose-free diet. After monitoring on the 21st day, the frequency of liquid bowel movements decreased to 2 times a day, and the appetite improved. **Conclusion:** Patients with radiation enteritis who are given probiotics may experience a reduction in symptoms of acute diarrhea. Direct administration of probiotics increases beneficial bacteria in the digestive tract.

### 1. Introduction

Endometrial carcinoma is a gynecological condition that is increasing in prevalence. GLOBOCAN cancer statistics for 2018 reported a total of 382,069 new cases and 89,929 deaths from cancer globally. Endometrial cancer ranks as the second most prevalent form of cancer and is the fourth highest contributor to mortality among gynecological cancers. It is projected to see 40% growth by the year 2040. Patients' age range typically falls between 55 and 62 years, with the highest occurrence observed at 62 years. Countries with high incomes have a higher incidence compared to low- to middle-income countries. Meanwhile, the death rate is rising among people in lower socioeconomic strata.<sup>1,2</sup>

Although up-front surgical staging is considered the standard of care in the treatment of endometrial

carcinoma, not all patients are deemed medically operable. Approximately 10% of patients are poor surgical candidates owing to obesity, advanced age, chronic medical conditions, and other factors. Hormonal therapy, such as megestrol acetate, is a viable option for these patients.<sup>11</sup> Another promising alternative for these patients is receiving up-front radiation therapy with or without chemotherapy, depending on staging and pathologic features. After treatment, the most commonly reported adverse effects were radiation enteritis, incontinence, bleeding, and weakness.<sup>3</sup>

Radiation enteritis is damage to the small and large intestines caused by radiation therapy for regional cancer treatment. The incidence is around 90% in patients undergoing radiation in the pelvic and abdominal regions. Acute events can occur from the



first day up to 90 days post-radiation, with symptoms such as diarrhea, nausea, vomiting, and abdominal cramps. If not properly treated, it can become chronic and lead to complications such as bleeding, perforation, stricture, fistula, abscess, and signs of sepsis. Probiotic therapy has been shown to benefit patients with radiation enteritis.<sup>4-6</sup>

The intestinal epithelial mucus is a protective layer, which is regulated by bacteria such as *Lactobacilli*, *Bifidobacteria*, and *Streptococci* which play a positive role in strengthening the intestinal mucosal barrier. Administration of *Lactobacillus* to healthy subjects significantly increases the scaffold protein ZO-1 and occludin in the vicinity of the tight junction structure, forming a cell side seal between the epithelial cells. Probiotics can also maintain micro-ecological stability and protect the intestinal barrier function by interrupting the pathogen's infection or inhibiting the growth of pathogens.<sup>7</sup>

## 2. Case Presentation

A 57-year-old morbidly obese woman has been experiencing vaginal bleeding for the past year. The patient exhibited vaginal hemorrhaging. After seeking medical attention, the recommendation was for the patient to undergo a hysterectomy and a pathological anatomy investigation. The results revealed the

presence of cervical cancer. 7 months ago, vaginal bleeding reoccurred. Subsequently, the patient sought medical care at the hospital and underwent an abdominal ultrasound, biopsy, and pathological investigation. The doctor raised the possibility of tumor recurrence and advised radiation and chemotherapy. The patient visited the radiation oncology department at Dr. Cipto Mangunkusumo National General Hospital one month ago, where they scheduled external beam radiation and brachytherapy.

On the 21st out of 25 radiation sessions and the 2nd chemotherapy session, the patient visited the nutrition clinic at the Radiation Oncology Therapy Center (IPTOR) with a complaint of a decrease in appetite and diarrhea for the past 5 days. The diarrhea occurred approximately 10 times a day, with each bowel movement being approximately 50 ml and yellow in color. The patient was then treated with anti-diarrheal therapy, 2 sachets of probiotics daily, each containing 10 million *Lactobacillus acidophilus*, *Bifidobacterium longum*, and *Streptococcus thermophilus*, zinc 20 mg once a day, and prescribed a low-fat and lactose-free diet. After monitoring on the 21st day, the frequency of diarrhea decreased, and the appetite improved (Figure 1).

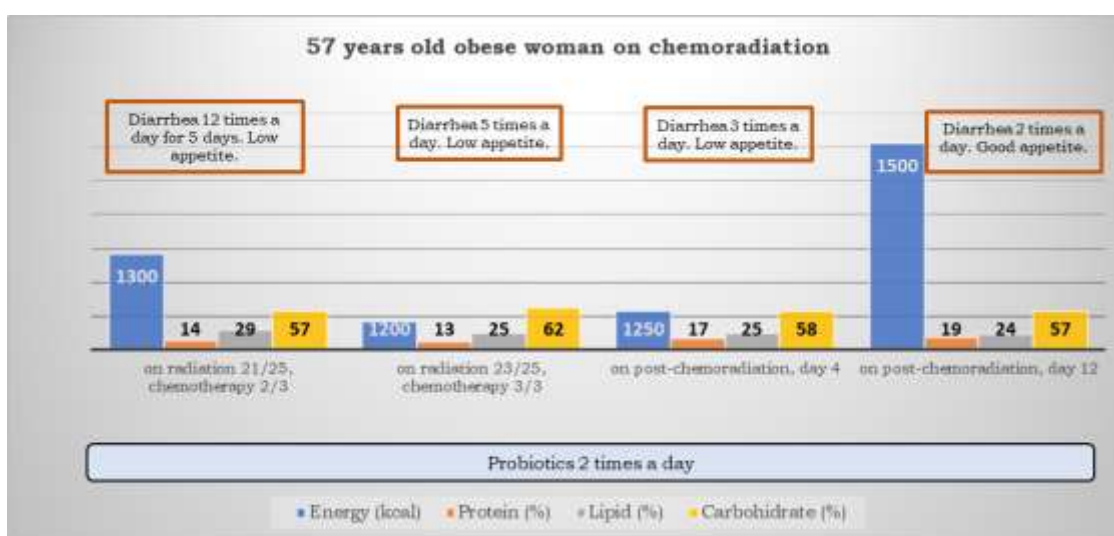


Figure 1. Follow up after probiotics supplementation.



### 3. Discussion

Radiation is a significant component in the therapy of various malignancies, typically in gynecological, urological, or rectal cases. Radiation is confined to the pelvic area where the benefits are maximized on target tissues and side effects on other organs are minimized. The application of external beam radiotherapy (EBRT) for cancer patients has increased in the last two decades. EBRT can enhance access to internal organs with intensity-modulated radiation therapy (IMRT) techniques. IMRT can reduce toxicity by minimizing damage to normal tissues through the delivery of varying doses to the radiation area. It is often administered to patients who are no longer operable. In patients at high risk of metastasis, adjuvant chemotherapy may be given. The goal of chemotherapy is to prevent relapse in distant organs, while radiation aims to prevent relapse in the pelvic area. Extended-field radiotherapy is indicated for patients with metastasis to the iliac lymph nodes or para-aortic nodes. If combined with chemotherapy, such as cisplatin, it may cause more severe hematological and gastrointestinal symptoms.<sup>8-10</sup>

In radiation-treated cancer patients, 90% experience gastrointestinal symptoms. Symptoms include changes in bowel movement patterns (94%), liquid bowel movements (80%), increased frequency of bowel movements (74%), and fecal incontinence (37%). These gastrointestinal symptoms result from inflammation in the intestines, contributing to a catabolic response that requires increased food intake to meet energy needs. Intestinal inflammation further contributes to malnutrition through severe diarrhea, abdominal pain, fever, and weight loss.<sup>11,12</sup>

The most common side effect is toxicity in the intestines, often referred to as radiation colitis. Acute events occur within 1 to 90 days, and beyond that, it is considered chronic. Enterocyte loss of mitotic ability, along with cell migration, leads to the loss of cells on the mucosal surface. This results in the impairment of water, macronutrients, and electrolyte

absorption, as well as a defense mechanism on the mucosa, leading to increased permeability to bacteria and antigens. Symptoms include diarrhea, abdominal pain, and tenesmus. Patients initially experience liquid bowel movements 2-3 times a day, which can worsen to 10 times a day.<sup>4,5</sup>

Radiation therapy also disrupts the colonization of diverse gut flora. Probiotics are products or preparations containing viable microorganisms in specific quantities that can provide beneficial effects for the host. Probiotics are a group of live microorganisms carefully selected, which, when provided in adequate amounts, offer health benefits to the body. It is recommended to consume  $10^8$ - $10^9$  CFU/g of probiotics. The functions of prebiotics include altering the composition of the microflora, thereby reducing the pH of the intestines, and enhancing the defense function in the intestines to prevent bacterial growth by producing antibacterial substances. Probiotics also decrease inflammatory responses in the intestines by improving the immune cell function, thereby restoring homeostasis in the intestinal mucosa. According to Chitapanarux et al., the administration of live *Lactobacillus acidophilus* and *Bifidobacterium bifidum* can reduce the incidence of radiation-induced diarrhea and decrease the need for anti-diarrheal medications. Studies show better results when a combination of strains is given rather than individual strains. Probiotics can reduce the occurrence of apoptosis in intestinal cells, accelerate the healing of radiation damage, and enhance both local and systemic immune systems against pathogens.<sup>6,13-19</sup>

### 4. Conclusion

Patients with radiation enteritis who are given probiotics may experience a reduction in symptoms of acute diarrhea. Direct administration of probiotics increases beneficial bacteria in the digestive tract.



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