

Letter to the Editor

Beyond probiotics: targeting the microbiota-metabolite axis in radiation-induced diarrhea

Sir,

We read with great interest recent reports addressing gastrointestinal toxicity in patients undergoing abdominal and pelvic radiotherapy. Radiation-induced enteritis and diarrhea remain clinically relevant complications that negatively affect quality of life and may compromise treatment adherence. Despite advances in radiotherapy techniques, effective preventive strategies remain limited.

Growing evidence highlights the bidirectional relationship between radiation injury and the gut microbiota. Radiation-induced dysbiosis has been associated with impaired epithelial regeneration, enhanced mucosal inflammation, and disruption of intestinal homeostasis. Consequently, probiotics have attracted considerable interest as a potential supportive care strategy.

Several randomized trials and systematic reviews have evaluated probiotic supplementation for the prevention of radiation-induced bowel toxicity. Although some studies have reported reductions in the incidence or severity of diarrhea, the overall evidence remains heterogeneous. Limitations include small sample sizes, variations in probiotic strains and dosages, and inconsistencies in study designs and clinical endpoints. Previous meta-analyses have emphasized these limitations and concluded that current evidence is insufficient to support routine probiotic use.^{1,2}

Accordingly, probiotic supplementation cannot currently be recommended as a standard preventive intervention for radiation-induced diarrhea in clinical practice. Large, well-designed randomized controlled trials using standardized probiotic formulations and clinically meaningful outcomes are required. Furthermore, although probiotics are generally considered safe, caution is warranted in immunocompromised or critically ill patients because of the potential risk of bloodstream infections.

Beyond direct probiotic supplementation, emerging evidence suggests that gut microbiota-derived metabolites may play a critical role in radiation-induced intestinal injury. Short-chain fatty acids (SCFAs), including butyrate, propionate, and acetate, as well as tryptophan-derived metabolites, contribute to intestinal homeostasis, epithelial barrier integrity, and regulation of inflammatory responses.³⁻⁵ SCFAs maintain intestinal function through activation of G protein-coupled receptors and inhibition of histone deacetylases, promoting regulatory T-cell

differentiation, preserving epithelial integrity, and modulating immune responses.^{5,6} These mechanisms may partly explain the biological effects attributed to probiotics and suggest that targeting microbiota-derived metabolites may represent a more precise therapeutic approach.

Recent experimental and translational studies further support the concept that radiation injury involves metabolic alterations in addition to microbial dysbiosis. In a ⁶⁰Co γ -ray-irradiated rat model, Zong et al demonstrated dynamic changes in plasma and fecal metabolites accompanied by alterations in gut microbial composition. Disrupted pathways included glycerophospholipid metabolism, α -linolenic acid metabolism, and unsaturated fatty acid biosynthesis.⁷ These findings reinforce the potential importance of the microbiota-metabolite axis in radiation-induced intestinal injury, although clinical translation remains to be established.

Collectively, current evidence suggests that radiation-induced dysbiosis may impair the production of protective microbial metabolites, thereby contributing to intestinal damage. While probiotics remain an attractive concept in supportive care, available evidence does not justify their routine use for preventing radiation-induced diarrhea. Future research should move beyond conventional probiotic supplementation and focus on standardized microbiota-targeted interventions and microbiota-derived metabolites. Such approaches may ultimately facilitate personalized strategies to reduce gastrointestinal toxicity and improve outcomes and quality of life in patients receiving pelvic radiotherapy.

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