No. 2230

The Role of Salt and Microbiota in the Pathophysiology of GVHD

Hideaki Fujiwara[1], Hisakazu Nishimori[1], Yoshinobu Maeda[2]

[1] Okayama University Hospital, Hematology and Oncology,
[2] Okayama University Graduate School of Medicine, Hematology, Oncology and Respiratory Meidcine

Summary

Allogeneic hematopoietic stem cell transplantation (alloHSCT) is a curative treatment for leukemia and other diseases. However, a serious complication, an immune reaction called graft-versus-host disease (GVHD), in which donor T cells attack normal organs, occurs in about 40% of patients and is the biggest barrier to a successful allogeneic transplant. About 80% of patients are temporarily unable to take oral intake due to anticancer agents or irradiation prior to allogeneic transplantation and receive total parenteral nutrition (TPN). Although oral intake becomes possible with recovery of mucosal damage, completion of dysbiosis and development of GVHD occur during this period, and oral and enteral nutritional therapy has been tried, but its efficacy is not clear. Among them, it is clear that sucrose-based nutrition promotes lymphocyte and neutrophil recovery, but the effects of salt (NaCl), which is abundant in the normal diet, on physiological functions and intestinal flora under alloHSCT are unknown. Excessive sodium chloride causes (1) a decrease of immunoregulatory T cells (Treg) and an increase of inflammatory Th17 cells (Th17), (2) a decrease of short-chain fatty acids by inducing dysbiosis of the intestinal microbiota similar to GVHD patients, (3) a decrease in gene expression due to histone deacetylation by decreasing short-chain fatty acids, and (4) immunosuppressive effects due to increased carbohydrate and steroid levels. Although various studies have examined the systemic effects of high-salt diets, the effects of zero salt intake on intestinal bacteria and systemic immunity are unknown. In mice with GVHD, adequate NaCl supplementation is more effective in reducing damage to intestinal tissues than to immune cells, suggesting that NaCl may reduce complications of alloHSCT with reduced damage to intestinal tissues. The lack of effects on immune cells suggests the possibility of a safer and more effective HSCT therapy that reduces GVHD, a normal tissue disorder, in an immunosuppression-independent manner while providing an antitumor effect by maintaining immune cell function, without the need for GVHD prophylaxis with immunosuppressive agents.