Prebiotics protect against acute graft-versus-host disease and preserve the gut microbiota in stem cell transplantation

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Key Points

- The intake of probiotics shortened the duration of oral mucositis and diarrhea, and reduced the incidence and severity of aGVHD.
- The microbial diversity, population of butyrate producers, and butyrate concentration were maintained in patients who consumed prebiotics.

Acute graft-versus-host disease (aGVHD) is a major cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Therefore, management of aGVHD is important for successful transplantation. Mucosal damage and alteration of the gut microbiota after allo-HSCT are key factors in the development of aGVHD. We conducted a prospective study to evaluate the ability of prebiotics, which can alleviate mucosal damage and manipulate the gut microbiota, to mitigate posttransplantation complications, including aGVHD. Resistant starch (RS) and a commercially available prebiotics mixture, GFO, were administered to allo-HSCT recipients from pretransplantation conditioning to day 28 after allo-HSCT. Prebiotic intake mitigated mucosal injury and reduced the incidence of all aGVHD grades combined and of aGVHD grades 2 to 4. The cumulative incidence of skin aGVHD was markedly decreased by prebiotics intake. Furthermore, the gut microbial diversity was well maintained and butyrate-producing bacterial population were preserved by prebiotics intake. In addition, the posttransplantation fecal butyrate concentration was maintained or increased more frequently in the prebiotics group. These observations indicate that prebiotic intake may be an effective strategy for preventing aGVHD in allo-HSCT, thereby improving treatment outcomes and the clinical utility of stem cell transplantation approaches. This study was registered on the University Hospital Medical Information Network (UMIN) clinical trials registry (https://www.umin.ac.jp/ctr/index.htm) as #UMIN000027563.

Introduction

Although allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a viable treatment of various hematological diseases, acute graft-versus-host disease (aGVHD) represents a major cause of morbidity and mortality.1 The standard first-line treatment of aGVHD is glucocorticoid (steroid), but a third to a half of patients do not respond to steroid therapy, and the long-term outlook for patients with steroid-refractory aGVHD is poor.2 Hence, management of aGVHD with alternative therapies is critical for a large proportion of allo-HSCT recipients.

An increasing body of evidence indicates that gut microbiota and their metabolites are closely associated with aGVHD. Translocation of bacterial components such as lipopolysaccharide is thought...