Dietary Changes May Improve Blood Cancer Outcomes

A high-fiber diet may slow multiple myeloma progression and lessen complications after a stem cell transplant, while a ketogenic diet could help CAR-T therapy work better.

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Simple and inexpensive dietary interventions could help improve outcomes among patients with various blood cancers, according to study results presented at the American Society of Hematology Annual Meeting (ASH 2024).

One study showed that a plant-based high-fiber diet may reduce complications after a stem cell transplant by improving the health of the gut microbiome, while another found that consuming more fiber may delay disease progression in people with smoldering multiple myeloma. A third study suggests that a ketogenic diet could boost the effectiveness of CAR-T therapy.

“One of the things we have greatest control over is our overall lifestyle and diet,” Chancellor Donald, MD, of Tulane University School of Medicine, said in an ASH news release.

Fiber Improves Graft-Versus-Host Disease

In the first study, Jenny Paredes, PhD, of City of Hope National Medical Center, and colleagues assessed the effects of a high-fiber diet on graft-versus-host disease (GVHD) after allogeneic donor stem cell transplantation in mice and humans.

Hematopoietic stem cell transplantation is a potentially curative option for certain blood cancers. These stem cells, which give rise to all types of blood cells, essentially replace the recipient’s malignant blood cells. One of the risks of an allogeneic transplant is GVHD, which occurs when immune cells derived from the donor’s stem cells attack the recipient’s body, causing mild to severe symptoms. Many people with GVHD have symptoms similar to those of irritable bowel disease.

Dietary fiber affects the intestinal microbiome—the ecosystem of bacteria and other microorganisms that live in the intestines—leading to increased microbial diversity and production of beneficial metabolites including short-chain fatty acids such as butyrate and acetate. Research has shown that a healthy microbiome is linked to reduced disease progression and better response to immunotherapy.

In a preclinical study, the researchers assessed fecal microbial composition, biomarkers, gene expression and survival in mice with GVHD who were fed a diet with varying quantities of cellulose, a type of fiber that mammals can't digest without the help of gut bacteria. Mice that consumed a fiber-rich diet (12% cellulose) had greater microbial diversity, decreased levels of certain pathogenic bacteria, greater butyrate production in the gut, a higher ratio of regulatory T cells, reduced inflammation and less damage to the gut lining compared with those that consumed a low-cellulose diet. These mice were also significant less likely to die of GVHD.

The researchers also collected dietary data from 173 allogeneic stem cell recipients treated at Memorial Sloan Kettering Cancer Center. Higher fiber consumption was significantly associated with greater gut microbiome diversity and higher levels of butyrate. What's more, people with high fiber intake had reduced likelihood of GVHD affecting their lower gastrointestinal tract and significantly better overall survival compared with those who ate little fiber.

"These results suggest that dietary fiber could be used in the prevention of GVHD," the research team concluded. This means that certain dietary restrictions commonly recommended after a stem cell transplant to reduce the risk of infections and bowel irritation—such as avoiding raw fruits and vegetables—may be counterproductive.

"Significant decrease of fiber intake during transplantation is detrimental—it's a lost opportunity to promote a healthy gut microbiome, recover from treatment-related microbiota injury and protect against GVHD," Parades said. She is now working to implement new nutrition protocols at City of Hope.

High Fiber Diet for Smoldering Myeloma

In the second study, Urvi A. Shah, MD, of Memorial Sloan Kettering Cancer Center, and colleagues assessed the benefits of a plant-based, high fiber diet for people with monoclonal gammopathy of undetermined significance (MGUS) or smoldering multiple myeloma, precursor conditions that can lead to active cancer of the bone marrow. MGUS and smoldering multiple myeloma are asymptomatic but characterized by abnormal proteins and blood cells. Prior research has shown that people with overweight or obesity are more likely to progress to multiple myeloma.

This analysis included 20 participants in the NUTRIVENTION trial who had a body mass index indicating overweight or obesity. During the first three months, they received ready-made meals and virtual nutrition coaching to encourage a diet rich in fruits and vegetables, beans, whole grains and nuts while avoiding animal products and processed foods. They could eat as much of these healthy foods as they wanted with no calorie restrictions. For the second three months, they continued to receive nutrition coaching while preparing their own meals. For the final six months, they received neither meals nor coaching.

The intervention was feasible, with patients reporting high adherence and moderate sustained weight loss. They showed improvement in biomarkers of insulin resistance, microbiome diversity and inflammation, and they reported improved quality of life. Two people showed reduced disease

progression, and none had progressed to multiple myeloma after one year, according to a Memorial Sloan Kettering news release.

“We saw improvements in all spheres, including metabolism, microbiome and immune system markers, and we also saw that two patients with progressive disease had the progression stabilize and slow down on the intervention,” Shah said. A larger follow-up trial is now underway.

These findings are supported by a preclinical study showing that mice with smoldering multiple myeloma that consumed a high-fiber diet had delayed disease progression. The high-fiber mice progressed to multiple myeloma in a median of 12 weeks versus 30 weeks for those on a low-fiber diet. All mice that received a standard low-fiber diet developed multiple myeloma, while about 40% of those on the high-fiber diet did not. Mice on the high fiber diet also showed greater gut microbiome diversity, more production of beneficial metabolites by gut microbes, reduced inflammation and improved immune function. These beneficial effects were seen in both lean and overweight mice and were independent of total calorie intake or weight loss.

This research “showcases the power of nutrition—specifically a high-fiber plant-based diet—and unlocks a better understanding of how it can lead to improvements in the microbiome and metabolism to build a stronger immune system,” Shah said. “These findings further support how we as physicians can empower patients, especially those with precancerous conditions, with knowledge on reducing their cancer risk through dietary changes.”

Keto Diet Boosts CAR-T Therapy

In the third study, Shan Liu, PhD, of the Perelman School of Medicine at the University of Pennsylvania, and colleagues looked at the effects of a ketogenic diet on the efficacy of chimeric antigen receptor T-cell therapy, better known as CAR-T.

This treatment involves removing a sample of a patient’s white blood cells, genetically modifying T cells to recognize and attack their cancer, manufacturing a large number of the modified cells in a laboratory and infusing them back into the body. CAR-T is approved for various types of leukemia and lymphoma.

The researchers first evaluated the effects of several different diets—including high-fiber, high-fat, high-protein, high cholesterol and ketogenic—on CAR T cells’ tumor-fighting ability in mice with B-cell lymphoma. A keto diet, which aims to make the body burn fat instead of carbohydrates, is low in fat, moderate in protein and high in carbs.

Mice that were fed a ketogenic diet showed the most tumor control and had the best overall survival after undergoing CAR-T therapy. Beta-hydroxybutyrate (BHB), a metabolite produced when consuming a keto diet, appeared to be the main driver of increased CAR T-cell activity. In fact, mice that were fed a standard diet plus a BHB supplement also showed improved CAR T-cell multiplication and better tumor control than those that didn’t receive the supplement, and a majority experienced complete remission.

The researchers suggest that BHB may increase CAR T-cell function by providing a more efficient source of energy than glucose, the typical fuel for most cells. When they added BHB to laboratory cultures of CAR T cells from people with lymphoma, T-cell expansion and mitochondrial function increased.

“Our theory is that CAR T cells prefer BHB as a fuel source rather than standard sugars in our body, such as glucose,” study coauthor Puneeth Guruprasad, PhD, said in a Penn Medicine news release. “So, increasing the levels of BHB in the body gives the CAR T cells more power to take out the cancer cells.”

Next, an analysis of blood samples from 17 patients who received CAR-T therapy for large B-cell lymphoma showed that higher BHB levels were linked to greater CAR T-cell expansion. Finally, the team analyzed T-cell function in healthy volunteers before and after they took a BHB supplement. Again, BHB appeared to enhance the function of T-cell mitochondria.

“Our research found that a ketogenic diet can enhance CAR T-cell function, and we further found that BHB, one of the important metabolites produced in response to a ketogenic diet, plays a major role in mediating this effect,” Liu said in the ASH news release. “Given that about two-thirds of patients who undergo CAR-T therapy either do not see a response or eventually relapse, a dietary intervention that could be implemented relatively easily along with CAR-T therapy would be very attractive.”

The researchers will soon launch a small Phase I clinical trial (NCT06610344) to evaluate BHB supplementation for patients with relapsed or refractory large B-cell lymphoma who are receiving commercially available CAR-T therapies. Until there’s more evidence, the study team advised against CAR-T patients trying a keto diet or BHB supplementation outside a research setting.

“We’re talking about an intervention that is relatively cheap and has low toxicity potential,” said study investigator Maayan Levy, PhD. “If the clinical trial data pans out, I’m excited to think about how a fairly simple approach like this could be combined with dietary interventions or other, more traditional, approaches to enhance the anticancer effect.”

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