

Side Effect Management in Lymphoma

Overview

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood, or other organs, and form a mass called a tumor. The body has two main types of lymphocytes that can develop into lymphomas: B lymphocytes (B cells) and T lymphocytes (T cells).

Side Effects of Treatments

Lymphoma is often painless and asymptomatic early on, but it can cause symptoms including swollen lymph nodes (for example, in the neck, armpits, or groin), fever, drenching night sweats, unintentional weight loss, fatigue, and discomfort, among other symptoms. Treatments for lymphoma, including chemotherapy, monoclonal antibodies, immunotherapy, radiation, and steroids often have side effects, although many treatments are very well tolerated. Each patient is different, so the side effects that occur and how severe they are may be different as well. Some patients experience many side effects and others have very few, but nearly all patients will experience some side effects, which may vary based on treatment; lymphoma type and stage; and the patient's age, other medical conditions, and overall health status. Although most side effects are temporary and resolve after therapy, they can cause a great deal of distress.

Chemotherapy drugs kill cancer cells, but these drugs may also kill healthy cells. When healthy cells in the bone marrow are killed, it can cause side effects such as *anemia* (low red blood cell counts); low platelet counts, which may increase the risk of bleeding; and low white blood cells counts, which decrease the ability of the immune system to fight infection, making patients more prone to infection.

Chemotherapy can be physically demanding and also cause:

- Changes in smell and taste
- Mouth sores
- Diarrhea
- Nausea and vomiting
- Fatigue
- Weight loss
- Hair loss

While *monoclonal antibodies* (engineered molecules that is not considered a chemotherapy) commonly have fewer side effects than most cancer treatments, they can affect normal cells as well as cancer cells. This can lead to an increased risk of infection, as well

as a variety of other side effects, including allergic reactions, fever, chills, weakness, headache, nausea/vomiting, diarrhea, low blood pressure, chest tightness, and rashes.

Besides monoclonal antibodies, other types of *immunotherapy* (treatments that help promote the body's immune response against the lymphoma), including antibody-drug conjugates, radioimmunotherapy (RIT), cytokines, immunomodulatory drugs (IMiDs), chimeric antigen receptor T-cell (CAR-T) therapy, and checkpoint inhibitors are also associated with various side effects. These may include anemia, arrhythmias, constipation, cough, diarrhea, fatigue, fever/chills, flu-like symptoms, itching, low blood cell counts, lung inflammation, neuropathy, nausea, pneumonia, rashes, shortness of breath, swelling, thinning hair, and upper respiratory tract infection.

Patients undergoing CAR-T therapy receive their treatment in the hospital where they can be closely monitored. Side effects include temporarily low blood cell counts, feeling tired (fatigue), and an increased risk of infection. In some patients, B cells are destroyed by the treatment in addition to the cancer cells, causing a condition called B-cell aplasia. B cells make antibodies that protect people from infections so when this happens, patients may need to periodically receive antibodies. The antibodies are given through a vein by intravenous infusion.

Two side effects that are potentially serious can occur after CAR-T therapy. These are cytokine release syndrome (CRS) and neurologic complications. CRS causes fever, rash, headache, and changes in blood pressure. Neurologic toxic effects can range from headaches to confusion, delirium, and seizures. The symptoms of CRS and neurological complications can occur within minutes or hours of beginning treatment, or may occur days to weeks later.

Radiation uses high-energy x-rays to kill cancer cells. Most side effects of radiation appear in the part of the body receiving the treatment, but radiation can also result in overall fatigue. Skin changes, such as pain, itching, or redness, almost always go away after radiation therapy is completed.

Steroids can cause a specific set of side effects including *insomnia* (not being able to fall asleep or stay asleep), increased appetite, mood/personality changes (feeling more irritable, angry, sad, or anxious than usual), weight gain, increased blood pressure, and increased blood sugar.

Diet

Diet is a key part of managing both lymphoma and the side effects of lymphoma treatment, as it provides the body with the nutrients and energy necessary for health. Many side effects can affect how patients feel about food and eating. Eating smaller meals more often rather than a few large meals each day may help patients feel less nauseous and make it easier to eat when appetite is diminished. Foods rich in carbohydrates such as starches can also help decrease nausea, whereas fatty foods may make nausea worse. Liquid nutritional drinks are a good way of getting enough vitamins and calories when patients have loss of appetite, nausea, or mouth sores. Drinking a lot of liquid is important for preventing dehydration, which often results from nausea, vomiting, and diarrhea.

During times when patients feel well enough to eat, a diet of fresh fruits and vegetables, protein, carbohydrates, and dairy products can help them increase and maintain their strength and energy and improve their body's healing ability.

Avoiding particular foods can ease some treatment side effects. For example, liquids or soft foods can make eating less painful if the patient has a dry mouth or difficulty swallowing solid foods. Also, certain foods may cause discomfort if patients have mouth sores from chemotherapy and radiation. Foods that are crunchy, salty, acidic (like citrus fruits), or spicy should be avoided. Dietary considerations are also important when a patient's sense of taste and smell changes. Some foods that were pleasurable before beginning cancer treatment may not be pleasurable during treatment and vice versa. It is important to experiment with different foods and find out what tastes good during treatment for lymphoma.

Dietary considerations are also important when white blood cell counts are low, which can result in the body having a harder time fighting infection. Avoid soft cheeses or cheeses with mold (such as brie, feta, or blue), and avoid raw or undercooked meat, fish, poultry, eggs, or tofu to reduce the risk of getting an infection. Wash fresh fruits and vegetables with soap to kill germs, and avoid fruits and vegetables that cannot be properly scrubbed and washed.

Vitamins and dietary supplements may affect lymphoma treatment. Patients should let their doctor know if they are taking any vitamins, minerals, or herbal supplements. In addition, alcohol may be very irritating if the mouth is sore during cancer treatment. It may also affect the body differently during treatment or even interact with the chemotherapy drugs. It is important for patients to discuss with their doctor whether drinking alcohol is safe in their particular circumstance. For more information, please view the *Nutrition* and the *Integrative Oncology* fact sheets on the Lymphoma Research Foundation's (LRF's) website at www.lymphoma.org/publications.

Lifestyle

Lymphoma and its treatments can cause fatigue. Changing routines may help accomplish daily tasks more easily. Prioritize the most important activities and let people who want to help do so. Planning chores or breaking down big tasks into smaller ones can help decrease tiredness. Remember that staying active and maintaining an exercise routine (as much as is comfortable) is vitally important for keeping the body as strong and energetic as possible. Also, taking the time to fit in short naps (20 to 30 minutes) may help recharge the body and mind during the day.

Intimate relationships may be affected during and following diagnosis and treatment for lymphoma. Intimacy is a very complicated issue that can be impacted by psychological factors (such as body image, desire, and emotional strain) as well as physical changes (such as fatigue, pain, dryness). Patients may experience changes in all, some, or none of the phases of sexual response (desire, arousal, orgasm, resolution). Open communication, time, and patience are important while finding the most helpful remedy. Patients should discuss with their healthcare team what sexual changes patients tend to experience during and after treatment and what can be done to prepare for and manage these changes if they occur.

If white blood cell counts are low as a result of chemotherapy, avoiding people who are coughing or sneezing can help reduce the risk of infection. Washing hands or using a hand sanitizer after visiting public places or touching items used by others is important. Patients should let their doctor know if they develop a fever during chemotherapy, as this may be a sign of an infection.

Cancer and cancer therapy may also affect thinking, memory, concentration, and attention. This is sometimes referred to as "chemo brain." Modest lifestyle modifications may be helpful, including making reminder lists, following structured routines, and, if necessary, delaying important decisions or tasks that require intense concentration. Exercising the mind with puzzles and brain teasers helps as well.

Medications and Products to Manage Side Effects

Nausea and vomiting are well-known side effects of chemotherapy and can sometimes be severe. Nausea and vomiting can prevent patients from doing the things they want to do, and they can even interfere with or halt treatment. For chemotherapy regimens that commonly cause nausea, anti-nausea medications (antiemetics) are often used preventively with each chemotherapy cycle. The goal is to prevent nausea from occurring in the first place. If nausea or vomiting does occur, it is important to take the anti-nausea medications

soon after symptoms start to prevent them from becoming severe. Patients should let their doctor know about their nausea or vomiting, as additional medications can be used to relieve and prevent both nausea and vomiting.

Both diarrhea and constipation can also be side effects of chemotherapy and radiation. These can also be prevented or treated with medication, so it is important that patients discuss these symptoms with their doctor or nurse as well.

Certain cancer treatments can result in mouth sores or ulcers in the lining of the mouth, gums, tongue, or lips. Dehydration, poor mouth care, oxygen therapy, alcohol or tobacco use, and insufficient nutrients may also cause sores. They can be painful and distressing and range from inconvenient to severe. Mouth sores can interfere with eating and drinking, and they can potentially become infected. Healing can take two to four weeks, which may interfere with the continuation of treatment. Although there is no guaranteed way to prevent mouth sores, there are ways to reduce the risk of getting them and mitigating their effects. Resolve any dental issues with a dentist before beginning chemotherapy, as they can worsen once treatment begins. After starting treatment, please notify your physician prior to having any dental procedures. Frequent mouth sores may be caused by a herpes simplex virus, which can be treated with antiviral medications. Staying hydrated by drinking two to three quarts of water each day can help prevent sores. Ice chips during treatment and for the first half hour following treatment can help reduce the risk of mouth sores following some types of chemotherapy. Drinking with a straw can help shield sensitive areas of the mouth. If it becomes difficult to use a soft bristle toothbrush due to sores and sensitivity, foam swabs are available to limit the irritation. Avoid mouthwash containing alcohol, as this may dry out your mouth. Salt water washes or a combination of baking soda and warm water can be used instead. Whitening toothpastes should be avoided, as they contain abrasives that can irritate sores.

Magnesium-based liquid medications (such as Maalox or milk of magnesia) can help promote healing of sores. Some medications such as palifermin (Kepivance) stimulate the growth of cells on the surface of the mouth and may help the sores recover more quickly. There are also medications that coat the entire lining of the mouth to form a film, protecting against sores and minimizing pain during eating and drinking. Topical painkillers containing benzocaine (such as Anbesol or Orajel) can also help to numb sore areas. Other medications are available to decrease the pain or discomfort caused by mouth sores. There are also products that can help ease dry mouth to prevent mouth sores that may result from activities like tooth brushing and flossing. Patients should discuss their oral

health with their doctor, dentist, and healthcare team prior to and during treatment to help prevent and manage any mouth sores that develop.

Insufficient sleep can impact energy levels, attention, cognitive function, and mood. Persistent insomnia has been associated with anxiety and depression. Insufficient sleep may also affect the immune system. Adequate sleep may even increase a person's pain tolerance. Many people with cancer experience sleep disturbances that can impact their quality of life. This can be due to pain, hospitalization, treatments, and/or the psychological impact of their disease. Difficulties with sleeping should be discussed with a doctor, as there are multiple approaches to improving sleep depending on the cause and the patient's preferences.

Not every medicine will work for everyone, but it is important to remember that there are many options, and it may take some time to find the right drug or treatment.

Protective Clothes and Accessories

Chemotherapy can make the skin more sensitive to sunlight and increase the risk of sunburns or rashes. Hats, scarves, and wigs reduce sun exposure in patients with hair loss and can lessen the distress associated with hair loss, which can negatively impact self-image. It is important to wear sunscreen on sun-exposed areas when planning to spend a prolonged period of time in direct sunlight.

Relaxation Techniques

Meditation, guided imagery, deep breathing, reading, yoga, and listening to music can provide distraction from symptoms and help patients overcome insomnia. Mindful relaxation techniques, such as meditation and yoga, are often helpful for accessing inner energy and directing thoughts toward healing and health. Guided imagery works to lessen tension in the body caused by worry and replace it with positive images that might reduce pain and other side effects. These methods have also been shown to aid the recovery process by improving mood, attitude, self-image, and outlook. For more information, please view the *Integrative Oncology* fact sheet on the LRF's website at www.lymphoma.org/publications.

Follow-up

Patients with lymphoma should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required at various times during *remission* (disappearance of signs and symptoms of lymphoma) to evaluate the need for additional treatment.

Some treatments can cause long-term side effects or late side effects, which can vary based on the duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these side effects during follow-up care. Visits may become less frequent the longer the disease remains in remission.

Patients and their caregivers are encouraged to keep copies of all medical records and test results as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any side effects resulting from treatment or potential disease recurrences. LRF's award-winning *Focus On Lymphoma* app (www.FocusOnLymphoma.org) can help patients manage this documentation.

Patient and Caregiver Support Services

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. One-to-one peer support programs, such as LRF's *Lymphoma Support Network*, connects patients and caregivers with volunteers who have experience with lymphoma or chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), similar treatments, or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this useful whether the patient is newly diagnosed, in treatment, or in remission.

Patient Education

LRF offers a wide range of opportunities to learn about lymphoma.

Ask the Doctor About Lymphoma is a national series of two-hour, topic-specific, community-based programs that combine a presentation by a medical doctor with an extensive question-and-answer session.

Lymphoma Workshops are regional, full-day educational programs that provide the latest information about lymphoma, current treatment options, and patient support issues.

The North American Educational Forum on Lymphoma is held annually and provides critical information on treatment options, patient support issues, and the latest in lymphoma research.

Webcasts are available on specific types of lymphoma, treatment options, and support topics.

Teleconferences are hour-long, interactive telephone programs that provide an opportunity to learn more about lymphoma, treatments, and promising research from leading lymphoma experts.

Patient Services and Support

The LRF Helpline staff members are available to answer your general questions about a lymphoma or CLL/SLL diagnosis and treatment information, as well as provide individual support and referrals to you and your loved ones. Callers may request the services of a language interpreter.

Patient Publications

LRF offers a series of print and digital patient education publications. LRF offers comprehensive guides on non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and the transplantation process in lymphoma, along with a variety of disease- and topic-specific fact sheets. Contact the LRF Helpline at (800) 500-9976 or visit our website at www.lymphoma.org/publications.

Mobile App

Focus On Lymphoma is the first mobile app that provides patients and caregivers comprehensive content based on their lymphoma subtype and tools to help manage their disease such as, keep track of medications and blood work, track symptoms, and document treatment side effects. The *Focus On Lymphoma* mobile app is available for download for iOS and Android devices in the Apple App Store and Google Play. For additional information on the mobile app, visit www.FocusOnLymphoma.org.

To learn more about any of these resources, visit our website at www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

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