Chemotherapy-induced peripheral neuropathy

Currently in Australia, 1 in every 2 men and 1 in every 3 women can expect to be diagnosed with cancer at some point in their lives. While in the past cancer was invariably fatal, in the last 100 years huge advances have been made in cancer treatment and support. New treatments have dramatically improved survival rates for cancer patients – with more than 66% of patients diagnosed with cancer surviving five years later. However, the long term side effects of cancer treatments are now a major issue which interfere with quality of life in cancer survivors.

Chemotherapy treatments are designed to attack cancer cells but these treatments typically produce additional side effects. One prominent side effect of chemotherapy treatment is nerve damage, which can be caused by chemotherapy drugs used for a variety of cancer types, including colorectal cancer, breast cancer, ovarian cancer and blood cancers. Chemotherapy-induced peripheral neuropathy (CIPN) is a type of nerve damage which usually affects the nerves in the hands and feet, causing symptoms of tingling, numbness and loss of sensation. Often these symptoms start in the toes or fingertips, but can progress up the arms and legs. As it gets worse, neuropathy causes problems with everyday activities, causing walking and balance problems and problems handling objects, leading to significant disability. Patients report that they have trouble typing, are unable to button clothes, are often stumbling and tripping, and experience other difficulties with everyday life.

Chemotherapy-induced peripheral neuropathy is a side effect of some of the most commonly used chemotherapies, including paclitaxel/docetaxel, oxaliplatin, cisplatin, vincristine, thalidomide and bortezomib. These chemotherapies are used to treat a range of cancer types, including breast, ovarian, lung, colorectal, testicular, head and neck and blood cancers. Nerve damage limits the amount of treatment that patients
can receive and may unfortunately result in irreversible, long-term damage. Sometimes nerve damage develops only late in treatment or even after the chemotherapy has stopped making it harder to identify and treat. The mechanisms underlying this nerve damage are not understood and there is no known effective treatment or cure.

**Focus on Oxaliplatin**

Oxaliplatin is a chemotherapy successfully used to treat bowel and rectal cancer in both early stage and advanced disease. However chemotherapy-induced peripheral neuropathy is an important side effect of oxaliplatin and can often lead to patients stopping treatment early due to the severity of their symptoms. Oxaliplatin produces two distinct types of neurotoxicity – acute and chronic.

Acute neurotoxicity develops immediately after oxaliplatin infusion and usually lasts for up to 7 days. Acute oxaliplatin-induced neurotoxicity produces unusual sensations such as tingling in the hands, feet and around the mouth. Often these symptoms are provoked by exposure to cold – patients report that their hands tingle when opening the refrigerator or walking outside on a cold day. Patients also report tingling in the mouth and lips after drinking a cold beverage. In a small number of patients, acute neurotoxicity produces a feeling of difficulty breathing or swallowing, after exposure to cold. In addition, some patients experience muscle cramps or twitching or spasms of the jaw. Some patients experience pain and stiffness in their jaw when eating, but usually only with the first bite. These symptoms can reoccur with every oxaliplatin treatment, but usually resolve within a week and do not usually cause patients to stop treatment.

As patients receive more chemotherapy treatments, chronic neurotoxicity is more likely to develop. Chronic neuropathy produces symptoms of tingling, numbness and lack of sensation in the fingers and toes. These symptoms are persistent and do not resolve in 7 days like acute oxaliplatin neurotoxic symptoms. Chronic neuropathy can cause problems with functional tasks including handwriting, computer typing, performing fine sewing work, buttoning clothes and holding chopsticks. Neuropathy in the feet can cause problems with driving and walking, leading to an increased risk
of balance problems and falls. Many patients who develop symptoms of chronic neuropathy during treatment receive a reduction in the oxaliplatin dose that they are given to attempt to reduce symptoms. A number of patients will stop oxaliplatin treatment early because the severity of their nerve symptoms. Even when patients stop receiving oxaliplatin treatment, nerve side effects can continue to worsen for several months.

Patients with chronic oxaliplatin-induced neuropathy often report that their symptoms improve and recover with time. However, in patients with moderate to severe neuropathy, neuropathic symptoms often persist. In addition, patients may adapt to neuropathy and change their behaviour to cope with the side effects. Objective nerve testing often demonstrates that neuropathy can be long lasting and persistent. There is currently no treatment or prevention for oxaliplatin-induced neuropathy, with the exception of reducing the dose or stopping treatment. A number of strategies have been tested to prevent or treat neuropathy, but none have been successful to date. More research is needed to understand the mechanisms that produce oxaliplatin-induced neuropathy and to enable the development of effective means to protect nerves from chemotherapy-induced damage.

References:


