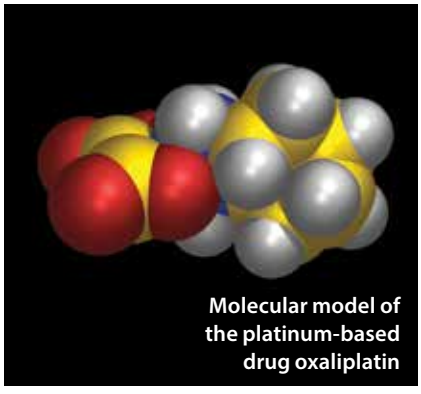

Molecular model of the platinum-based drug oxaliplatin

Neurotoxicity from oxaliplatin

What are some of the potential autonomic issues related to acute neurotoxicity from oxaliplatin?
— Sandy Pollock, RN

Oxaliplatin is a platinum alkylating agent most frequently used in combination with an antimetabolite, such as one of the fluoropyrimidines (eg, 5-FU/fluorouracil, capecitabine [Xeloda]) or gemcitabine (Gemzar, generics). These combinations are used to treat various GI cancers, including colorectal cancer. One of the most notable adverse effects of oxaliplatin is neuropathy, with more than 90% of patients experiencing some type of neuropathy during their course of treatment.[1] Oxaliplatin is associated with two types of neuropathy. Acute neuropathy manifests soon after oxaliplatin is administered and resolves within 5 to 10 days after the dose. Chronic neuropathy typically manifests after patients have received multiple doses of oxaliplatin and does not resolve between cycles.

Acute neuropathy can occur within minutes to a day after receiving oxaliplatin, and is often triggered by cold. Symptoms typically consist of paresthesia (tingling, pins-and-needles sensation), dysesthesia (abnormal sensation), and hypoesthesia (reduced sensation). This neuropathy may also be associated with shortness of breath or difficulty swallowing; unusual sensations in the tongue, jaw, or laryngospasms; eye pain; and muscle spasms or cramps. Chronic neuropathy, on the other hand, is cumulative and occurs more frequently in patients who have received total doses of 540–850 mg/m^2 or more of oxaliplatin.[2] Symptoms of chronic neuropathy may include paresthesia, dysesthesia, and hypoesthesia in addition to changes in proprioception (affecting movements that require fine motor coordination such as writing). Chronic neuropathy generally improves over several months after oxaliplatin is discontinued.

There are multiple theories regarding exactly how oxaliplatin causes neuropathy.[1,2] Animal models suggest that oxaliplatin may cause motor and sensory nerve hyperexcitability, resulting in acute neuropathic symptoms. Chronic neuropathy may be caused by accumulation of platinum compounds in the dorsal root ganglia cells. Contributing factors may include the stress caused by prolonged nerve hyperexcitability, and mitochondrial damage caused by oxaliplatin.

The autonomic nervous system controls involuntary body functions, such as heart rate and digestion. Although most cases of oxaliplatin-induced neuropathy do not affect autonomic functions, there are some case reports of patients experiencing autonomic neuropathy-like symptoms after receiving oxaliplatin.[3] The symptoms reported in these cases included proprioception deficiencies, urinary retention, and Lhermitte sign (an electric sensation experienced when flexing the neck). In all of these cases, the patients had previously received more than 1,000 mg of oxaliplatin.

Patients should be monitored for neuropathic symptoms when receiving oxaliplatin. Acute neuropathies should resolve prior to administering the subsequent dose, and both acute and chronic neuropathies should be graded to assess the need for dose adjustment or holding of oxaliplatin. Symptoms of autonomic neuropathy should be reported immediately. Symptoms that may also be suggestive of an allergic reaction should be reported and managed immediately. ■

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