

Managing Chemotherapy-Induced Neuropathy

Chemotherapy-induced peripheral neuropathy is a significant cause of cancer-related pain. Unfortunately, there presently is little that can be done to prevent it, according to Patrick M. Dougherty, MD, PhD, Professor of Anesthesiology and Pain Medicine, The University of Texas M.D. Anderson Cancer Center, Houston, Texas.

Over 50% of cancer patients experience pain, and about 35% of oncology patients have severe pain. In many cases, pain results from peripheral neuropathy that develops after chemotherapy. Agents most likely to cause this condition are paclitaxel, vincristine, cisplatin, oxaliplatin (Eloxatin), and bortezomib (Velcade).

“Bortezomib compromises the most nerve function,” he noted. “But regardless of the compound, patients who develop peripheral neuropathy end up with the same final pain condition. If it becomes chronic, it is hard to get patients back to baseline, and it is difficult to manage,” he said.

At its worst, pain from chemotherapy-induced peripheral neuropathy exceeds a rating of 7 on a 12-point visual analog scale. “Pain this bad is very significant. A level above 7 can be incapacitating,” Dr. Dougherty pointed out. “Even a pain level of 5 would leave us wanting to stay at home.”

The pain is localized in the extremities. Distally, it follows a “stocking-and-glove-type” pattern. It is felt in three areas: the more painful (“worst symptom”) area, the border area (area of transition), and the “normal” area. Patients describe the pain as something like “rats biting,” particularly when their fingers and toes are affected. In addition, the pain is felt in the palms and soles of the feet, where patients usually report “pins and needles.” Most patients add that the pain tends to stop at the wrists or ankles.

Trophic changes, including finger-

clubbing and edematous, swollen extremities, may accompany these symptoms. In extreme cases, patients may experience blanching and ischemia that leads to gangrene.

Chemotherapy-induced peripheral neuropathy is accompanied by a profound impairment of touch that is demonstrated by several tests. Quantitative sensory testing shows the touch threshold to be significantly higher with chemotherapy exposure than at baseline. The test involves placing a graded filament on the skin’s surface and asking patients to indicate when they feel it. Patients at baseline and unaffected persons will feel pressure at 0.1 g/mm²; however, patients receiving certain chemotherapeutic agents report sensations that are 10 times more powerful, Dr. Dougherty said.

This impairment in small, myelinated fibers is substantial; pinprick threshold tests used to evaluate A β fiber function show deficits extending to the normal skin and traveling up the forearm. In addition, the ability to detect sharpness via A Δ fibers is impaired; this change in sensation is important to patients.

Skin temperature also is affected by chemotherapeutic agents. Baseline skin temperature is approximately 34°C in controls, but it drops to below 32°C in the most painful involved areas after paclitaxel and cisplatin use and to just over 30°C after vincristine and bortezomib administration.

“Patients’ fingertips feel cold, and this suggests something—maybe an autonomic dysreflexia underlying the condition,” Dr. Dougherty suggested.

Pain thresholds related to temperature also are significantly altered during chemotherapy, especially with regard to warm sensations, which involve unmyelinated C fibers. Whereas control subjects report warm sensations at approximately 36°C, patients with neuropathy

sense warm temperatures at 39°C–45°C, depending upon the chemotherapy agent they received. Less effect on heat-pain sensations has been noted.

Cool and cold-pain thresholds involve small myelinated A δ fibers. Control subjects experience cool sensations at approximately 20°C; however, patients with neuropathy feel such sensations at 10°C–17°C in the most painful areas.

“Patients with paclitaxel-induced peripheral neuropathy, interestingly, get a paradoxical burning sensation to the cooling of the skin,” he noted, adding, “Patients often tell you they avoid open-

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—Patrick Dougherty, MD, PhD

ing the freezer or going down the freezer aisle of the grocery store. They really have problems dealing with the cold.”

Regarding treatment, Dr. Dougherty stated, “This is a search for the best drug for each patient.” Options include gabapentin, pregabalin (Lyrica), and tricyclic antidepressants. Pregabalin is best for chronic, well-established neuropathic pain and is less effective for acute pain, he added.

Little can be done about neuropathy. Once it is established, however, can it be prevented? Dr. Dougherty’s advice to patients was, “Stay away from things that are bad for your nerves.” This includes overconsumption of alcoholic beverages and contact with organophosphates and mosquito spray, gasoline fumes, and other substances. He also encouraged consumption of a diet rich in antioxidants. “Hopefully, we will eventually have a robust, mechanism-driven intervention,” he said.