Medical Xpress

The ups and downs of incorporating a new treatment to try to prevent chemotherapy-associated neuropa

September 21 2015

In this age of the 24-hour news cycle, instant access to all information everywhere, PubMed, LinkedIn, Facebook, Twitter and hundreds of other ways to glean and share knowledge beyond the traditional stack of printed journals delivered to their door, physicians continue to struggle to arm themselves with the most effective therapies.

Fast access to information may result in practice change; however, subsequent data may disprove effectiveness and require even more practice change. The cycle may continue over several years and several studies, with the potential for missed information growing with each practice-change decision.

In a study released today in the *Journal of the National Comprehensive Cancer Network*, Mayo Clinic researchers, looking at one drug used for one condition, show how, even in a fairly narrow field with limited general consumer involvement, the quick penetration of information resulted in several practice shifts and reversals across the nation that stretched over a decade. The researchers looked at the timeline and impacts of various events on the use of calcium magnesium (CaMg) for oxaliplatin-induced neuropathy.

The timeline

- 2001 *Journal of Neurophysiology* article provides a possible

explanation for the neurotoxicity of oxaliplatin.

- 2002 *ASCO Proceedings* abstract describes use of CaMg infusions for prevention of oxaliplatin-induced neuropathy.
- 2004 *Clinical Cancer Research* article further describes results initially presented in the ASCO Proceedings abstract, reporting the discontinuation of oxaliplatin due to neurotoxicity in 31 percent of patients who had not received CaMg in prior years, but only in 4 percent of patients who more recently had.

Result: Many oncologists start routinely administering intravenous CaMg to patients receiving oxaliplatin (used in up to 40 percent of courses), and several prospective randomized trials launch.

- 2007 *Journal of Clinical Oncology* letter to the editor reports that the data monitoring committee for one of these studies (the CONcePT trial) had identified a lower disease response rate in patients receiving CaMg, resulting in early study closure.

Result: Use of CaMg drops exponentially, and related trials close early.

- 2008 *Journal of Clinical Oncology* letter to the editor reports that the data monitoring committee for the CONcePT trial had been incorrect, and there had not been any true decrease in response rates in patients receiving CaMg.

Result: Use of CaMg rebounds.

- 2009 Results of an abstract presentation at the ASCO Annual Meeting show CaMg decreased cumulative sensory neurotoxicity, but did not affect oxaliplatin-induced acute neuropathy from one of the early closed trials (N04C7). The results are noted as preliminary. A new trial, N08CB, launches to obtain more data, since the N04C7 trial closed prematurely.

- 2011 *Journal of Clinical Oncology* article generates renewed enthusiasm for use of CaMg, showing some positive results of the N04C7 trial.
- 2013 An ASCO Annual Meeting abstract presentation and Journal of Clinical Oncology article show results of N08CB demonstrated convincingly negative results.

Result: Use of CaMg to treat oxaliplatin-induced neuropathy drops exponentially.

The data

This study looked at the Mayo Clinic practice (1,457 patients from January 2003 through June 2014) and the national rates of CaMg usage obtained from the OptumLabs Data Warehouse (41,165 patients during the same period). In both settings, the pattern showed adoption in 2003, cessation in 2007, readoption in 2008, and cessation in 2013.

Why does it matter?

Physicians want to alleviate suffering and heal their patients. Clinical researchers face continuous challenges to identify ways to improve outcomes and quality of life for patients and find the most effective ways to translate their findings into everyday usage. Research addresses questions physicians seek to answer; however, early findings can be contradictory, and publicity levels vary, making it difficult for physicians to sort through the vast amounts of information available to determine best practices. And, it takes a very long time for clinical research to be completed to the point that the results are considered proven without doubt.

"When faced with a major clinical problem for which few treatments are

available, rapid changes in practice based on preliminary data may be more common," says Charles Loprinzi, M.D., oncologist and senior author of the study. "We all want to give our patients the best possible care, and sometimes the lack of definitive data is judged to be less important than the perceived benefits for patients."

It becomes a calculated risk, based on what information patients and physicians have available at the moment of decision, to try a new therapy.

"In some cases, early adopters of a new treatment are congratulated for their wise foresight, because they save lives and/or improve quality of life for many patients even before final data are reported," says study co-author and fellow oncologist Axel Grothey, M.D. "In other cases, early adopters of a new treatment may cause net harm." He and his fellow researchers caution that the desire to find the therapy that will improve patient outcomes can result in unexpected and sometimes serious consequences.

"As with all treatment decisions, the whole picture must be considered," Dr. Loprinzi says. "In addition to examining the evidence supporting particular therapeutic options, we must consider each individual patient's genetic makeup, medical history and personal preferences when determining the appropriate course of action."

In the case of CaMg use, when the definitive data was in, it did not show any beneficial effect in reducing oxaliplatin-induced neuropathy. But, it also did not appear to cause much harm other than the time and expense to give the therapy.

The lesson here might be not so much for physicians, who work with the information they have available, but for the medical research community. More funding for medical research is necessary to

accelerate translation. When it takes a decade to get to an acceptable level of proof, many stops in between have the potential to derail productive research and potentially cause harm through administration of treatments that won't help or by withholding treatments that are eventually shown to work, while waiting for final research studies to be complete.

Provided by Mayo Clinic