Dear OncoLink "Ask The Experts,"

A family member was recently diagnosed with esophageal cancer. One of the chemotherapy treatments mentioned was Fluorouracil. We've read that if a person is DPD-deficient, the side effects could be severe, including death. Is there a test for this? Is this rare? Or should he avoid this drug completely? We've found articles on the internet that lead us to believe between 10% - 15% of the population have this deficiency.

Weijing Sun, MD, Assistant Professor of Medicine at the University of Pennsylvania, the Director of Upper GI and Pancreatic-biliary-hepatic Cancer Group and the Associate Director of the GI Cancer Program, responds:

Fluorouracil (5-FU) has been in use as a chemotherapy drug for more than 50 years. Overall, it is a safe drug, with relatively mild side effects in most patients.

DPD (aka Dihydropyrimidine dehydrogenase) is an enzyme that is necessary for the metabolism or breakdown of more than 80% of the 5-FU dose received. A lack of properly functioning DPD can lead to severe side effects, which tend to occur sooner than expected with functioning DPD.

'DPD deficiency' has been estimated by some to occur in 10% of all patients, but most studies have found 3-5% to be the actual incidence. The actual amount of functioning DPD varies widely in these patients, leading to variations in the amount and severity of side effects. Many of these can be prevented by adjusting the dose of 5-FU. Only 0.1-0.2% of the population has a complete lack of DPD, which would lead to the most severe toxicity. Although DPD levels can be tested, this testing is not typically performed or suggested at this point, but is an area of ongoing research. Researchers are looking at various tests that could be done to detect this abnormality, but feel that the currently available test is lacking in sensitivity and specificity.

Some researchers are looking at blocking DPD completely, making every patient completely deficient, allowing for better absorption of 5-FU, and making dose adjustments easier.

An interesting finding in some studies was that patients with lower levels of DPD had better responses to the chemotherapy when compared with patients with higher levels of DPD, who had poor responses to therapy. In another study looking at prescreening for abnormalities in the DPD gene, there were 300 patients in whom the authors could find no abnormalities. Despite this, 20 of these patients (6.6%) had severe side effects, suggesting that DPD is not the only culprit in 5-FU toxicity.

References & Further Reading


Morel, A et al., Clinical relevance of different dihydropyrimidine dehydrogenase gene single nucleotide polymorphisms on 5-fluorouracil tolerance. Mol Cancer Ther 2006 5(11): 2895-2904

Van Kuilenberg, AB et al., Clinical Implications of Dihydropyrimidine Dehydrogenase (DPD) Deficiency in Patients with Severe 5-Fluorouracil-associated Toxicity: Identification of New Mutations in the DPD Gene Clinical Cancer Research 2000 Vol. 6, 4705-4712

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No
diagnosing or treating a health problem or a disease. It is not a substitute for professional care. If you have or suspect you may have a health problem or have questions or concerns about the medication that you have been prescribed, you should consult your health care provider.