Dosing Chemotherapy in Obese Patients: No Clear Answers, Yet

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Almost one third of Americans are currently considered obese. As the number of patients with cancer who are overweight is increasing, the conventions of chemotherapy dosing are constantly being questioned. Because of the concern for overdosing obese patients, clinicians are routinely tasked with questions such as—Should we use actual body weight, ideal body weight, or something in between? Should we cap doses? Overdosing patients is a concern for all clinicians, but underdosing may be just as problematic. Therefore, we must consider the dose-reduction questions in light of the medical literature, which suggests that such reductions may compromise patient outcomes.

The use of body surface area (BSA) for dosing chemotherapy was developed in the 1950s as a method to translate animal dosing into humans, but no scientific study has demonstrated that BSA is a better dosing measurement than body weight or even fixed doses of chemotherapy. Many pharmacokinetic (PK) studies have demonstrated that the PK parameters do not correlate with BSA, and a growing body of evidence suggests that dosing obese patients based on actual body weight is not associated with increased toxicity. Some have suggested that flat dosing of carboplatin based on population parameters is just as effective as dosing based on the area under the curve (AUC) calculation.

In this issue of the *Journal of Hematology Oncology Pharmacy*, Nightingale and colleagues address the issue of dosing carboplatin in obese patients. This retrospective analysis involves overweight patients receiving carboplatin. The authors’ approach in this study is to look at toxicity, which is supposed to be minimized with AUC-based dosing. The conclusion that the use of actual body weight to estimate the glomerular filtration rate (GFR) is associated with high incidence of toxicity is misleading. We know the incidence of toxicity in the 20 obese patients, but normal-weight patients were excluded from this study. How can we know, then, that there would not have been a similar rate of toxicity in normal-weight patients? Of note, the 2 patients whose creatinine clearance was capped at 125 mL/min did not have toxicity. We are, therefore, left with the question of how to calculate the appropriate dose in overweight patients.

The common complaint about all studies that examine the effects of obesity on dosing is that those studies are usually retrospective, with small sample sizes, and the patient variability in PK parameters makes any generalized statement difficult. Most often, the goals of therapy are not considered. Furthermore, a little toxicity may be a good thing.

Clinicians spend too much time worrying about doses of chemotherapy. The assumption is that because doses are individualized based on the BSA calculation or the AUC, a more accurate dose is being selected. The reality is, however, that all the dosing calculations are based on an estimate.

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The good news is that help may be on the way. The American Society of Clinical Oncology is in the process of developing a practice guideline for dosing chemotherapy in obese patients with cancer. Until then—perhaps even beyond that—clinicians will need to balance the risks versus benefits and the efficacy versus toxicity, because the answer to the question of dosing in obese patients is still not clear.

Author Disclosure Statement
Dr Soefje is on the Speaker’s Bureaus of Amgen, Eisai Pharmaceuticals, and ICU Medical, Inc.
References