Introduction to Dosing Medications in Obese Patients

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Outline

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Obesity Pandemic

Worldwide obesity has doubled since 1980, accounting for 13% of adults.[1] In the United States, more than one-third of adults and 17% of children are obese, and almost one-half of non-Hispanic blacks and 43% of Hispanics are obese.[2] The high prevalence of obesity is impacting the United States healthcare system, costing $147 billion in 2008.[3] Overconsumption of calorically-dense foods, physical inactivity, genetics, psychological underlying conditions, and personality traits contribute to the rise in obesity. Individuals of low socioeconomic status are at an even higher risk because they are unable to afford healthy foods or do not have the education to make good choices.

Obesity puts individuals at high risk for cardiovascular disease as well as diabetes, hypertension, stroke, and angina, and it has been linked to breast, gastrointestinal, esophagus, colorectal, liver, stomach, pancreas, gallbladder, and genitourinary cancers.[4,5] The excessive weight causes pressure to be put on bones and joints, which causes osteoarthritis to occur at a younger age. Unfortunately, obesity continues to worsen and has been impacting individuals and the entire healthcare system. This chapter will discuss measures of weight, pharmacokinetic and pharmacodynamic changes in obese patients, as well as pharmacologic treatment of obesity.

Measures of Weight and Obesity

It is important to assess for trends prior to assuming a weight for calculating a medication dose. A patient's weight can fluctuate depending on volume status and/or diuresis, especially in the critically ill. Knowing whether the weight was a standing or bed weight can help you fully understand the accuracy of the measurement. Some obese patients are not able to stand so the bed weight may be the only means to obtain a weight. Patients with heart failure, kidney failure on dialysis, and ascites as well as pregnant women are just some of the populations to consider. Patients with cancer can gain or lose weight throughout their cycles so it is important to reevaluate weight each cycle.

Body mass index (BMI) is standard for categorizing obesity. Adolphe Quetelet developed the Quetelet index, also known as *BMI*, dating back to 1832.[6] BMI (**Equation 1-1**, **Table 1-1**) was later found to be a good determinate of subcutaneous body fat but not percentage body fat.[6,7] The World Health Organization defines adults with a BMI between 25 and 29.99 kg/m^2 as overweight and BMI >30 kg/m^2 as obese. Obese patients are further divided into subclassifications of class I, class II, and class III for a BMI of 30 to 34.99 kg/m^2, 35 to 39.99 kg/m^2, and ≥40 kg/m^2, respectively.[8] Although BMI has been shown to correlate with subcutaneous fat, use caution when applying BMI to individuals with greater muscle mass, women, or the elderly as BMI may not be the best descriptor.

In addition to BMI as described above, body surface area (BSA) and percent body fat are additional ways to quantify an individual's size. BSA is another index that will be discussed in Chapter 6: Dosing Antineoplastic Medications in Obese Patients. Bodybuilders are an example of when the BMI may be skewed. Their weight would be higher because muscle is more dense than fat so BMI would be falsely elevated. Additionally, the BMI equation was validated prior to the marked increase in obesity rates; thus, percent body fat would better describe a person of such build. Percent body fat is performed by dividing the free-fat mass, which is the mass excluding any fat, by the person's total body weight (TBW). There are many ways to determine free-fat mass such as hydrodensitometry, skin-fold measurement, bioelectrical impedance analysis, and dual-energy x-ray absorptiometry.[9] All of these methods, including the gold standard hydrodensitometry, require sophisticated equipment that limits the use for widespread implementation. Percent ideal body weight (IBW) and BMI are readily available and is easy to calculate; however, BMI remains the standard.

Little information is available from pharmaceutical manufactures as to what body weight is recommended and the study's population weight distribution. Most commonly, TBW is utilized for weight-based drug dosing. **Figure 1-1** shows size descriptors and how they relate to one another in regard to amount of fat included. Free-fat mass[7] (**Equations 1-2a** and **1-2b**, **Table 1-1**) excludes essential fat, whereas lean body weight (LBW) takes into account fat in cell membranes, bone marrow, and central nervous system (**Equations 1-3a** and **1-3b**, **Table 1-1**).[10] LBW was developed for determining patient size for epidemiological reasons, but it appears to be a more appropriate means of estimating weight in obese patients because it does not decline with increasing TBW compared to IBW.[9] However, some have argued LBW may not be the best descriptor in patients who are significantly overweight because the population initially studied was not as severely obese as the current population.[11] Both LBW and IBW incorporate sex into the calculations, but they differ in that LBW includes BMI whereas IBW is based solely on height.[12] IBW was derived from Metropolitan Life Insurance Company of New York Data (**Equations 1-4a** and **1-4b**, **Table 1-1**).[12] IBW came from the optimal weight for those with the greatest life expectancy, not based on pharmacokinetic studies. However, the IBW equation has been widely studied for aminoglyco-