Stony Brook University Hospital Antimicrobial Stewardship
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Stony Brook Medicine

SBUH Antimicrobial Dosing Guide for Patients with Obesity

Definitions and Equations

$$BMI = \frac{\text{weight (kg)}}{\text{height}^2\ (m^2)}$$

WHO BMI Classification	Definition
Obese Class I and II (obese)	BMI 30-40 kg/m^2
Obese Class III (morbidly obese)	BMI ≥ 40 kg/m^2

A.) Background[1]:

Body Weight	Equation
IBW (kg) **Ideal body weight**	Male: 50 kg + 2.3 x (every inch above 60 inches) Female: 45.5 kg + 2.3 x (every inch above 60 inches)
AdjBW (kg) **Adjusted body weight**	IBW + 0.4 x (TBW – IBW)
TBW (kg) **Total Body Weight**	Measured Weight

1.) Drug dosing in patients with obesity remains challenging due to limited high-quality evidence. Pharmacokinetic changes in patients with obesity are frequently reported but can be variable and sometimes conflicting. These changes don't always translate to differences in clinical outcomes but are used to inform dosing strategies. In addition, increases in volume of distribution (Vd) are generally observed because of increased adipose and lean muscle mass. Vd may be overestimated if based on TBW if the drug does not enter adipose tissue well (e.g., hydrophilic drugs). Factors other than lipophilicity and Vd affect dosing in obesity. For example, maintenance doses are mostly driven by total body clearance (Cl), which is the sum of the clearances by each of the eliminating organs (primarily the liver and kidneys). Increased organ mass in obesity may influence clearance. Increased renal clearance was attributed to increased kidney mass and renal blood flow in obesity, and it may affect the elimination rate. Extended infusions, high doses, and therapeutic drug monitoring are important strategies for optimizing dosing in patients with obesity. Most studies included small patient populations and were retrospective in nature. Additional studies are needed to clinically validate proposed dosing strategies

Table 1: Recommended Antibiotic Dosing in Obesity (BMI ≥ 30 kg/m^2)

Drug	Dose	Comments
Acyclovir[2,3]	BMI ≥30-40 kg/m^2: Use IBW BMI ≥40 kg/m^2: Use AdjBW	No difference in AKI rates with AdjBW compared to IBW dosing[2] BMI ≥40.0 kg/m2 patients treated with I.V. acyclovir dosed by IBW experience substantially decreased overall

		exposure compared to normal weight patients dosed by total body weight[3]
Aminoglycosides[4] (Amikacin, Gentamicin, Tobramycin)	Dose based on AdjBW Adjust as needed by therapeutic drug monitoring Utilize SBUH Aminoglycoside Dosing Guidelines	Using ideal body weight alone might result in subtherapeutic concentrations, particularly in patients with morbid obesity (BMI >40 kg/m^2). • Approximately 40% of the aminoglycoside dose is distributed into adipose tissue Using total body weight in patients with obesity could lead to supratherapeutic levels and increased risk of toxicity
Amoxicillin[1] +/- Clavulanate	Amoxicillin: 1g PO every 8 hours Amoxicillin/clavulanate: 875mg/125mg PO every 8 hours	Consider the upper limit of normal dosing for severe or deep-seated infections
Amphotericin (Liposomal)[5,6]	Dose based on AdjBW for BMI >40 kg/m^2 Total Body Weight dosing can be considered for life threating infections and/or critically ill (caution with doses > 5mg/kg/day) Consider using a fixed dose cap for patients ≥100 kg: • For 3 mg/kg dosing, use a fixed dose of 300 mg • For 5 mg/kg dosing, use a fixed dose of 500 mg For doses > 5mg/kg/day - maximum daily dose of 600 mg is recommended	A pharmacokinetic study in morbidly obese individuals (BMI >40 kg/m^2) found that body size had no effect on clearance of Liposomal Amphotericin B (L-AmB). This supports using fixed dosing rather than weight-based dosing in patients with morbid obesity.[5] One clinical study comparing AdjBW vs TBW dosing of L-AmB in patients with obesity found similar efficacy outcomes, but potentially improved safety with AdjBW dosing.[6]
Cefazolin[7,8,9]	Pre-op: If patient >120 kg - 3 grams.[9] Perioperatively: If patient >120 kg - 3 grams Q4 can be utilized during operation.[9] Max studied dose is 2g Q6 if Creatinine Clearance (CrCl) > 215 ml/min.[8]	Consider upper limit of normal dosing in severe infections (e.g., up to 2 g q8h or 1.5–2 g q6h intermittent dosing)[7] In post trauma critically ill patients, data suggest 2 g q6h if CrCl> 215 ml/min[8]
Cefepime[1]	Dose on TBW up to 2g IV Q8. BMI>40 kg/m^2: Extended infusion over 3 hours is preferred.	Extended infusion is also preferred for life-threatening infections caused by resistant pathogens (e.g., minimum inhibitory concentrations approaching 8

		mg/L), with infection-site penetration limitations, or for critically ill patients with augmented renal function
Colistin[10,11]	Dose Based on IBW.[11]	When actual body weight was used, the risk of nephrotoxicity was particularly high in patients with predictors of nephrotoxicity that include a BMI of ≥31.5 kg/m2 (independently).[10] The 30-day mortality rate was 40% in the nephrotoxicity-positive group versus 14% in the nephrotoxicity-negative group.[10]
Daptomycin[1,12]	Dose based on AdjBW	When using TBW in patients with obesity, clinical data suggests significant increases in AUC, $C_{max,}$ and a higher incidence of adverse reactions (e.g., elevated CPK, myalgias).[1] Clinical failure and 90-day mortality were statistically equivalent when comparing TBW to AdjBW dosing strategies for daptomycin.[12] Caution in renal insufficiency, dialysis. Monitor CKs and signs of myopathy
Fluconazole[13,14]	Dose based on TBW. Maximum dose is not well established (800 mg to 1.6 grams). Daily doses up to 1.6 g are well tolerated.[14]	Candidiasis: a loading dose of 12 mg/kg followed by a maintenance dose of 6 or 12 mg/kg/day is required to achieve either the low or high PK/PD target.[13]
Flucytosine[15]	Dose Based on IBW, then adjust by level.	In a retrospective study: Initial peak levels were supratherapeutic in 10/19 cases (53%). Of those 10 patients, 70% were overweight/obese, and 60% would have received a lower initial dose if IBW had been used with dose rounding to the nearest 500mg capsule. Those with supratherapeutic levels had higher rates of new onset hepatic and renal dysfunction, 30% and 90% respectively. In 32% of cases, using IBW would have resulted in a lower daily dose.[15]
Foscarnet[16]	Dose based on AdjBW	Recommendations are not provided in the prescribing information regarding dosing in patients with obesity. Due to its hydrophilic nature, major risk of

		nephrotoxicity and other adverse effects, it may be prudent to utilize IBW or AdjBW.[16]
Ganciclovir[16,17]	Dose based on AdjBW	Ganciclovir dosing in patients with obesity is not addressed in the prescribing information. Due to the hydrophilic nature of ganciclovir and its similarity in size (277 Da), action and toxicity to acyclovir, utilization of IBW when calculating doses in patients with obesity could be considered on a case-by-case basis.[16] Utilization of AdjBW ganciclovir dosing did not result in decreased neutropenia or treatment efficacy as compared to TBW dosing.[17]
Meropenem[1,23]	The patient's CrCl and critical illness status is more clinically significant than their BMI in determining if extended infusion or increased dose is needed. BMI appears to have a minimal effect on PK/PD target attainment in critically ill patients, while increasing CrCl (calculated using TBW) values were strongly associated with lower PK/PD target attainment rates.[23] For patients with less severe infections or infections caused by non-Pseudomonas pathogens with a minimum inhibitory concentration ≤1 mg/L, may consider 1 g every 8 hours over 30 minutes Higher doses (2g IV Q8 over 30 mins) or prolonged infusions (1 g IV Q8 or 2g IV Q8 infused over 3 hours) should be utilized in the following scenarios in critically ill patients: • CrCl > 150ml/min for non-obese.[23] • CrCl >100 ml/min and obese.[1] • Concerned for infection with less susceptible pathogens such as Acinetobacter	At higher CrCl levels (≥150 ml/min) in critically ill patients in all BMI groups, intermittent meropenem dosing regimens consistently failed to achieve PK/PD targets. This failure could be remedied by adjusting either the dose (2g IV Q8) or the duration of infusion (over 3 hours). Specifically, meropenem at 500 mg or 1,000 mg q8h did not achieve the PK/PD target for the EUCAST breakpoint for A. baumannii and P. aeruginosa of a MIC of 2 mg/liter. When the doses were escalated to 2,000 mg q8h, the PK/PD target was achieved. Similarly, when meropenem was administered as a prolonged infusion (3 h), PK/PD target achievement increased significantly, even for lower doses of 500 mg q8h.[23]

	baumannii and Pseudomonas aeruginosa (i.e., MIC >2 mg/L)	
Polymixin B[18,19]	Limited Data. Consider using AdjBW, especially with the upper end of dosing range. Consider Max dose of 249 mg to limit risk of toxicity, although not clinically validated.[18]	Monte Carlo simulation indicated that ABW-based regimens could achieve adequate exposure with a lower risk of toxicity when compared to TBW-based regimens and the fixed dose of 125 mg or 150 mg would have a high probability of toxicity. Probability of target attainments results revealed that TBW, ABW, and IBW-based regimens had comparable results.[18] For the obese population, AdjBW-based regimens but with a daily dose <250 mg would be the optimal regimen to improve polymyxin B therapeutic efficacy and reduce the incidence of nephrotoxicity with the MIC ≤0.5 mg/L.[18] Clinicians should exercise caution with the suggested approach of dosing polymyxin B on TBW, especially among patients at the extremes of TBW.[19]
Sulfamethoxazole/ Trimethoprim[1,20]	Dose based on AdjBW Maximum: 320 mg [trimethoprim component]/dose.[1] Maximum dose of 960 mg (trimethoprim component)/day.[20]	Consider adjusted body weight when using high doses (e.g., >8 mg/kg/day).[1]
Vancomycin[1,21]	Dose loading doses based on TBW Maximum loading dose 3 grams[21] • SBUH Vancomycin Dosing Guidelines for Adult Patients: maximum loading dose of 2 grams. Consider an initial maximum daily dose of 4.5 grams.[21]	Adjust as needed by therapeutic drug monitoring Maintenance doses: Utilize SBUH Vancomycin Dosing Guidelines for Adult Patients and PrecisePK history to tailor dosing • Can consider utilizing AdjBW CrCl rather than IBW CrCl for critically ill patients

Voriconazole	Dose based on AdjBW	Adjust as needed by therapeutic drug monitoring AdjBW-based voriconazole dosing significantly improved rates of therapeutic trough attainment compared to TBW-based dosing in patients weighing ≥120% of their IBW.[22]

Beta Lactam antibiotics and obesity: Most beta lactam antibiotics are dosed based on TBW up to a maximum dose. In the setting of obesity and critically ill patients, consider utilizing the maximum range of dosing and extended infusions if applicable. For example, meropenem can be dosed up to 2 g IV every 8-hour extended infusion over 3 hours, and cefepime can be dosed up to Up to 2 g IV every 8-hour extended infusion over 3 hours.[1]

Disclaimer: If using an antimicrobial not listed, consult other literature for weight-based dosing evidence (Example: LexiComp). If nothing is mentioned, utilize TBW for dosing.

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