Controversies & Conundrums in Obesity

Nancy Balch, PharmD
Senior Attending Pharmacist
Massachusetts General Hospital

Objectives
- Differentiate between antibiotic dosing, and administration, in obese patients versus normal weight patients

Abbreviations
- VD: Volume of Distribution
- CL: Clearance
- PK: Pharmacokinetic
- BMI: Body Mass Index
- IBW: Ideal Body Weight
- TBW: Total Body Weight
- PNWT: Predicted Normal Weight
- LBW: Lean Body Weight
- AJBW or ABW: Adjusted Body Weight

Obesity, a growing epidemic
- Earlier estimate: > 1/3 (>78 million) US adults obese
- Initial data: surgery did not help lifespan/ QOL
- Newer data: surgery benefits

WHO Estimates
- 2014: >600 million adults, over 18, obese
- 2014: >1.9 billion adults, over 18, overweight
- 2013: 42 million children < 5, obese
- Increasing: ‘under-developed’ Countries

Body Mass Index
- Based solely on height versus weight
- Muscle mass artificially inflates BMI
- On-line calculators available on many sites
- Different BMI scales
- If studies don’t match your patient’s BMI, caution with data
Adult BMI Used by Many Studies

<table>
<thead>
<tr>
<th>Underweight: less than 19</th>
<th>Ideal: 19 to 25</th>
<th>Overweight: 25 to 30</th>
<th>Obese: greater than 30, Severely Obese: greater than 35</th>
<th>Morbidly Obese: greater than 40, Super Obese: greater than 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 19</td>
<td>19 to 25</td>
<td>25 to 30</td>
<td>30 to 35</td>
<td>35 to 40</td>
</tr>
<tr>
<td></td>
<td>40 to 50</td>
<td>&gt; 50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI: match the patient!

A. 70”, 138 lb, BMI: 19.8
B. BMI 25 < 30
C. 64”, 230 lb, BMI: 39.5

Studies
- Most: small numbers of patients
- Need: multi-site studies for large numbers
- Verify: numbers at end of study match numbers required to see a difference
- Retrospective: less reliable than prospective
- May see additional changes with weight reduction surgery (ie not normalized)
- Need studies on this population

Antibiotic Studies
- Often under-dosed, ICU pts: VD higher
- Lipophilic: TBW (higher load than maint)
- Hydrophilic: IBW/ABW
- Check levels when able
- Many studies did not include those with comorbidity

Available Adult Data

<table>
<thead>
<tr>
<th>Medication</th>
<th>Date</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycosides</td>
<td>Weak</td>
<td>f LD AJBW, then renal f/t levels (ABW high, BW low)</td>
</tr>
<tr>
<td>Beta lactams</td>
<td>Weak-Mod</td>
<td>Higher doses required, AJBW or ABW</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>Weak-Mod</td>
<td>4 hr infusion, upper limit of dosing</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Weak-Mod</td>
<td>High end of dosing, prophylaxis for surgery (2 to 3 gm). Studies primarily in weight loss surgery and pregnancy.</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Weak</td>
<td>Upper end of dosing</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Weak-Mod</td>
<td>Upper end of dosing, old data– outdated?</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Weak</td>
<td>Upper end of dosing, old data– outdated?</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>Weak</td>
<td>Appears different PK/PH</td>
</tr>
</tbody>
</table>

Available Adult Data

<table>
<thead>
<tr>
<th>Medication</th>
<th>Date</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ertapenem</td>
<td>Week</td>
<td>Conflicting data regarding dose (4 hr infusion)</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Week</td>
<td>Higher end of dosing, lower tissue concentrations</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Week</td>
<td>Continuous infusion, 1 BW, AJBW</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Week</td>
<td>Undetermined</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Week</td>
<td>Upper end of dosing, 4 hr infusion</td>
</tr>
</tbody>
</table>
Available Adult Data

<table>
<thead>
<tr>
<th>Medication</th>
<th>Data</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>Moderate</td>
<td>4 hr infusion</td>
</tr>
<tr>
<td>Quinupristin/Dalfopristin</td>
<td>Weak</td>
<td>TBW, with capf</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Moderate</td>
<td>Nomogram, max dosing, use levels</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>Weak</td>
<td>Conflicting data</td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>Weak</td>
<td>160 mg bid (unless decreased renal fct)</td>
</tr>
</tbody>
</table>

Key Takeaways

- Majority of antibiotic data, in obese patients: weak
- Use ABW dosing recommendation if data lacking
- Create Multidisciplinary Committee for dosing plans on all populations
- While data remains limited in pediatric patients, decision tools available

Post-Test

In regards to antibiotics in obese adult patients:

A. As long as renal and hepatic function are normal, no dose change is required
B. Dosing information should be separated by BMI category, but data is lacking.
C. Antibiotics that are not fat-soluble never require dose changes in obese adults.
D. Patients with a BMI > 50 must be dosed on actual body weight for antibiotics, because their infections are so difficult to treat

Pediatrics: take home info

- Limited pedi data, less on obese pedi
- Cannot 'class' dose meds without data
- Extra caution: narrow therapeutic range
- Load doses: ABW or TBW, break up load (ie narrow therapeutic range
- Maintenance doses: IBW

Pediatrics: take home info

- Decision tool recommended
- Create decision support tool, based on current tools
- Prioritize medications to review
  - Determination of weights (ie TBW, ABW, IBW, LBW)
  - Determine scoring

Pediatrics: take home info

- Sites FOR REVIEW, that may be useful:
  - [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3018176/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3018176/)
Drug Dosing in Obesity Reference Table

An evidence-based drug dosing resource.

Dosing weight-based medications in obese patients can often be a tricky proposition. Most medications do not have guidelines for morbid obesity, forcing clinicians to pursue in-depth literature searches in order to decide on a dose.

The purpose of this page is to serve as a dynamic, growing repository of evidence-based recommendations regarding medication dosing in obese patients. I would encourage you to examine each medication’s cited references in order to form your own conclusions. As always, reasonable clinical judgment is required in conjunction with this information.

Lastly, if you have primary literature regarding obesity dosing for a medication that is not listed on this table, please contact me with the drug name and citation and I would be happy to add it to the list.

Acyclovir

1. Dose using ideal body weight (per package insert)

No information about dose adjustments in extremely obese patients exists.

References


